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NEWS 7 Apr 22 PROSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 11 New e-mail delivery for search results now available
NEWS 10 Jun 11 MEDLINE Reload
NEWS 11 Jun 11 POTFULL has been reloaded
NEWS 12 Jul 02 FORGOR no longer contains STANDARDS file segment
NEWS 13 Jul 23 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 29 NETFIRST to be removed from STN
NEWS 16 Aug 26 CANCERLIT reload
NEWS 17 Aug 26 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 Aug 26 WPIX has been reloaded and enhanced
NEWS 19 Aug 26 JAPIO to be reloaded August 26, 2002
NEWS 20 Aug 29 Aquatic Toxicity Information Retrieval (AQUIRE)
now available on STN
NEWS 21 Aug 29 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 22 Aug 29 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 23 Aug 26 Sequence searching in REGISTRY enhanced

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
CURRENT MACINTOSH VERSION IS V6.0a(ENG AND V6.0Ja(JP),
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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1-7/1/02

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=> s (oxidant or oxidative) (w) stress
L1 119419 (OXIDANT OR OXIDATIVE) (W) STRESS

=> s (polymerize or polymerized or polymerization) (w) (peptide or polypeptide or protein)
4 FILES SEARCHED...
L2 968 (POLYMERIZE OR POLYMERIZED OR POLYMERIZATION) (W) (PEPTIDE OR POLYPEPTIDE OR PROTEIN

=> s l1 and l2
L3 1 L1 AND L2

=> d l3 all

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2002:143824 CAPLUS
DN 136:181182
TI Assessment of **oxidant stress** in vitro and in vivo
IN Kim, Hyoshoo; Roberts-Kirchoff, Elizabeth Starr
PA USA
SO U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM C12Q001-26
ICS G01N033-53
NCL 435023000
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 14
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002022244	A1	20020221	US 2001-915776	20010726
PRAI US 2000-221651P	P	20000728		

AB There is provided a method of assessing **oxidant stress** by measuring polym.. of proteins. Also provided is a marker for

oxidant stress which includes a **polymd.** **protein.** A kit for use in assessing **oxidant stress**, the kit including an assay for detecting **polymd.** **proteins** is also provided. A method of lowering **oxidant stress** by administering to a patient an effective amt. of at least one reducing agent is also provided. A pharmaceutical compn. for lowering **oxidant stress**, the pharmaceutical having an effective amt. of reducing agent and a pharmaceutically acceptable carrier is also provided.

ST **oxidant stress**

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Nitrated, polymd.; assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(polymd.; assessment of **oxidant stress** in vitro and in vivo)

IT Biomarkers (biological responses)
Composition
Disulfide group
Drugs
Nitration
Oxidation
Oxidative stress, biological
Oxidizing agents
Polymerization
Reducing agents
Reduction
Test kits
(assessment of **oxidant stress** in vitro and in vivo)

IT Dimers
RL: ANT (Analyte); ANST (Analytical study)
(assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(assessment of **oxidant stress** in vitro and in vivo)

IT Drug delivery systems
(carriers; assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(disulfide bonded polymd.; assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(nitrated disulfide bonded polymd.; assessment of **oxidant stress** in vitro and in vivo)

IT 19059-14-4, Peroxynitrite
RL: ANT (Analyte); ANST (Analytical study)
(assessment of **oxidant stress** in vitro and in vivo)

IT 9007-43-6D, Cytochrome c, nitrated, polymd. 27025-41-8, Oxidized glutathione 39391-18-9, Prostaglandin h2 synthase 39391-18-9D, Prostaglandin H2 synthase, nitrated, polymd.
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

09901880

(assessment of **oxidant stress** in vitro and in vivo)
IT 39391-18-9, Prostaglandin H2 synthase, nitrated dimer
BL: PSU (Biological study, unclassified); BIOL (Biological study)
(assessment of **oxidant stress** in vitro and in vivo)
IT 70-18-8, Reduced glutathione, biological studies 9007-43-6, Cytochrome c, biological studies
BL: PSU (Biological study, unclassified); PCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(assessment of **oxidant stress** in vitro and in vivo
IT 105234-97-4, Peroxynitrate
BL: RCT (Reactant); RACT (Reactant or reagent)
(assessment of **oxidant stress** in vitro and in vivo

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	21.61	21.82
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=> S 70021-41-8 RN

L4 1 70021-41-8/RN

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STNSEARCH
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=> FIL BIOSIS MEDLINE CAPLUS EMBASE SCISEARCH
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FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 16:51:09 ON 28 AUG 2002
L1 119419 S (OXIDANT OR OXIDATIVE) (W) STRESS
L2 365 S (POLYMERIZE OR POLYMERIZED OR POLYMERIZATION) (W) (PEPTIDE OR
L3 1 S L1 AND L2

FILE 'REGISTRY' ENTERED AT 16:53:41 ON 28 AUG 2002
L4 1 S 7002-41-5/RN
SET NOTICE 1 DISPLAY
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FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 16:54:23 ON 28 AUG 2002

=> s l1 and (prostoglandin or cytochrome)
L5 1 L1 AND (PROSTOGLANDIN OR CYTOCHROME)

=> s l5 1 ab so ar t. py
MISSING OPERATOR L5 1 AB
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l5 ab so ar t. py
MISSING OPERATOR L5 AB
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

09/03/01

09921660

=> d l5 ab so au ti py

L5 ANSWER 1 OF 1 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Eicosanoids accumulation and formation of oxygen free radicals have been implicated in the pathogenesis of ischemia/reperfusion brain injury. In the present study, we examined whether green tea extract protects against ischemia/reperfusion-induced brain injury by minimizing eicosanoid accumulation and oxygen radical-induced oxidative damage in the brain. Green tea extract (0.5%) was orally administered to Wistar rats for 3 weeks before induction of ischemia. Ischemia was induced by the occlusion of middle cerebral arteries for 60 min and reperfusion was achieved for 24 h. Infarction volume in the ipsilateral hemisphere of ischemia/reperfusion animals was 114 .+-. 16 mm(3) in the 0.5% green tea pretreated animals compared to 180 .+-. 54 mm(3) in left hemisphere of nontreated animals. Green tea extract (1.5%) also reduced ischemia/reperfusion-induced eicosanoid concentration: Leukotriene C(4) (from 245 .+-. 61 to 66 .+-. 23), **prostoglandin** E(2) (from 366 .+-. 71 to 212 .+-. 43) and thromboxane A(2) (327 .+-. 69 to 281 .+-. 97 ng/mg protein). Ischemia-reperfusion-induced increases of hydrogen peroxide level (from 698 .+-. 76 to 901 .+-. 89 nmole/mg protein), lipid peroxidation products (from 1010 .+-. 110 to 320 .+-. 70 nmole/mg protein) and 8-oxodG formation (from 1.5 .+-. 0.3 to 0.8 .+-. 0.2 ng/.mu.g DNA, x10(-2)) were also reduced. Moreover, 0.5% green tea extract also reduced the apoptotic cell number (from 44 .+-. 11 to 23 .+-. 7 in the striatum, and from 72 .+-. 11 to 42 .+-. 5 apoptotic cells/high power field in the cortex region). Green tea extract pretreatment also promoted recovery from the ischemia/reperfusion-induced inhibition of active avoidance. The present study shows that the minimizing effect of green tea extract on the eicosanoid accumulation and oxidative damage in addition to the reduction of neuronal cell death could eventually result in protective effect on the ischemia reperfusion-induced brain injury and behavior deficit. Copyright .COPYRGT. 2001 Elsevier Science Inc.
SO Brain Research Bulletin, (2000) 53/6 (743-749).
Refs: 27
ISSN: 0361-9230 CODEN: BRBUDU
AU Hong C.I.; Ryu S.R.; Kim H.J.; Lee J.K.; Lee S.H.; Kim D.B.; Yun Y.P.; Ryu C.H.; Lee E.M.; Kim P.Y.
TI Neuroprotective effect of green tea extract in experimental ischemia-reperfusion brain injury.
PY 2000

=> s (oxidant or oxidative) (w) (stress or damage)
L6 137254 (OXIDANT OR OXIDATIVE) (W) (STRESS OR DAMAGE)

=> s l6 and l2
L7 1 L6 AND L2

=> d so au py ab 1-1 l7

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
SO U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
IN Kim, Hyesook; Roberts-Kirchoff, Elizabeth Starr
PY 2002
AB There is provided a method of assessing **oxidant stress** by measuring polymn. of proteins. Also provided is a marker for **oxidant stress** which includes a **polymd. protein**. A kit for use in assessing **oxidant stress**, the kit including an assay for detecting **polymd. proteins** is also provided. A method of lowering **oxidant**

stress by administering to a patient an effective amt. of at least one reducing agent is also provided. A pharmaceutical compn. for lowering **oxidant stress**, the pharmaceutical having an effective amt. of reducing agent and a pharmaceutically acceptable carrier is also provided.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
SO Contributions to Nephrology (1995), 112(Dialysis-Related Amyloidosis), 11-17
CODEN: CNEPDO; ISSN: 0302-5144
AU Cheng, Rong-zhu; Kawakishi, Shunno
PY 1995
AB The authors investigated in detail the protein damages, esp. polymn., that arise by the action of glycated peptide, N.epsilon.-fructoselysine (FL), glucosone and cupric ion. Some of the results suggest that the polymn. may have arisen from a radical reaction that initiated in the glucosone/cupric ion/oxygen complex.

=> s (oxidant (or oxidative) (w) (stress or damage)
L8 137259 (OXIDANT OR OXIDATIVE) (W) (STRESS OR DAMAGE)

=> d hist

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FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 16:51:09 ON 28 AUG 2002
L1 119419 S (OXIDANT OR OXIDATIVE (W) STRESS
L2 565 S (POLYMERIZE OR POLYMERIZED OR POLYMERIZATION) (W) (PEPTIDE OR
L3 1 S L1 AND L2

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L4 1 S 27021-41-8 FN
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FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 16:54:23 ON 28 AUG 2002
L5 1 S L1 AND (PROSTOGLANDIN OR CYCTOCHROME)
L6 137259 S (OXIDANT OR OXIDATIVE (W) (STRESS OR DAMAGE)
L7 1 S L6 AND L2
L8 137259 S (OXIDANT OR OXIDATIVE (W) (STRESS OR DAMAGE)

=>
=> s l8 and l1
L9 1 L8 AND L5

=> s l8 and (PROSTOGLANDIN OR CYCTOCHROME)
L10 4 L8 AND (PROSTOGLANDIN OR CYCTOCHROME)

=> d l10 1-4 ab au so ti

L10 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB Eicosanoids accumulation and formation of oxygen free radicals have been implicated in the pathogenesis of ischemia/reperfusion brain injury. In the present study, we examined whether green tea extract protects against ischemia/reperfusion-induced brain injury by minimizing eicosanoid accumulation and oxygen radical-induced **oxidative damage** in the brain. Green tea extract (0.5 %) was orally administered to Wistar rats for 5 weeks before induction of ischemia. Ischemia was induced by the

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occlusion of middle cerebral arteries for 60 min and reperfusion was achieved for 24 h. Infarction volume in the ipsilateral hemisphere of ischemia/reperfusion animals was 114 +- 16 mm3 in the 0.5 green tea pretreated animals compared to 180 +- 54 mm3 in left hemisphere of nontreated animals. Green tea extract (0.5 also reduced ischemia reperfusion-induced eicosanoid concentration: Leukotriene C4 (from 241 +- 51 to 186 +- 32), **prostoglandin** E2 from 306 +- 71 to 213 +- 43) and thromboxane A2 (327 +- 69 to 251 +- 67 ng/mg protein). Ischemia/reperfusion-induced increases of hydrogen peroxide level (from 688 +- 76 to 501 +- 99 nmole/mg protein), lipid peroxidation products (from 1010 +- 111 to 742 +- 70 nmole/mg protein) and 8-oxodG formation (from 1.5 +- 0.3 to 0.8 +- 0.2 ng/mg DNA, X 10-2) were also reduced. Moreover, 0.5 green tea extract also reduced the apoptotic cell number (from 44 +- 11 to 29 +- 1 in the striatum, and from 72 +- 11 to 42 +- 5 apoptotic cells/high power field in the cortex region). Green tea extract pretreatment also promoted recovery from the ischemia/reperfusion-induced inhibition of active avoidance. The present study shows that the minimizing effect of green tea extract on the eicosanoid accumulation and **oxidative damage** in addition to the reduction of neuronal cell death could eventually result in protective effect on the ischemia/reperfusion-induced brain injury and behavior deficit.

AU Hong, Jin Tae (1); Ryu, Seung Eel; Kim, Hye Jin; Lee, Jong Kwon; Lee, Sun Bok; Kim, Dae Byung; Yun, Yeo Pyo; Ryu, John Hoon; Lee, Byung Ha; Kim, Pu Young

SO Brain Research Bulletin, (December, 1998) Vol. 46, No. 6, pp. 743-749. print.
ISSN: 0361-9230.

TI Neuroprotective effect of green tea extract in experimental ischemia-reperfusion brain injury.

L10 ANSWER 2 OF 4 MEDLINE

AB Eicosanoids accumulation and formation of oxygen free radicals have been implicated in the pathogenesis of ischemia reperfusion brain injury. In the present study, we examined whether green tea extract protects against ischemia/reperfusion-induced brain injury by minimizing eicosanoid accumulation and oxygen radical-induced **oxidative damage** in the brain. Green tea extract (0.5%) was orally administered to Wistar rats for 3 weeks before induction of ischemia. Ischemia was induced by the occlusion of middle cerebral arteries for 60 min and reperfusion was achieved for 24 h. Infarction volume in the ipsilateral hemisphere of ischemia reperfusion animals was 114 +/- 16 mm(3) in the 0.5% green tea pretreated animals compared to 180 +/- 54 mm(3) in left hemisphere of nontreated animals. Green tea extract (0.5% also reduced ischemia reperfusion-induced eicosanoid concentration: Leukotriene C 4) (from 241 +/- 51 to 186 +/- 32), **prostoglandin** E(2) (from 306 +/- 71 to 213 +/- 43) and thromboxane A(2) (327 +/- 69 to 251 +/- 67 ng/mg protein). Ischemia/reperfusion-induced increases of hydrogen peroxide level (from 688 +/- 76 to 501 +/- 99 nmole/mg protein), lipid peroxidation products (from 1010 +/- 111 to 742 +/- 70 nmole/mg protein) and 8-oxodG formation (from 1.5 +/- 0.3 to 0.8 +/- 0.2 ng/mg DNA, x10 -2) were also reduced. Moreover, 0.5% green tea extract also reduced the apoptotic cell number (from 44 +/- 11 to 29 +/- 1 in the striatum, and from 72 +/- 11 to 42 +/- 5 apoptotic cells/high power field in the cortex region). Green tea extract pretreatment also promoted recovery from the ischemia/reperfusion-induced inhibition of active avoidance. The present study shows that the minimizing effect of green tea extract on the eicosanoid accumulation and **oxidative damage** in addition to the reduction of neuronal cell death could eventually result in protective effect on the ischemia/reperfusion-induced brain injury and behavior deficit.

AU Hong J T; Ryu S R; Kim H J; Lee J K; Lee S H; Kim D B; Yun Y P; Ryu J H;

Lee B.M.; Kim H.Y.
SO BRAIN RESEARCH BULLETIN, (2000 Dec) 53 (6) 743-9.
Journal code: 7605831. ISSN: 0361-9230.
TI Neuroprotective effect of green tea extract in experimental ischemia-reperfusion brain injury.

L10 ANSWER 3 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AB Eicosanoids accumulation and formation of oxygen free radicals have been implicated in the pathogenesis of ischemia/reperfusion brain injury. In the present study, we examined whether green tea extract protects against ischemia/reperfusion-induced brain injury by minimizing eicosanoid accumulation and oxygen radical-induced **oxidative damage** in the brain. Green tea extract (0.5%) was orally administered to Wistar rats for 3 weeks before induction of ischemia. Ischemia was induced by the occlusion of middle cerebral arteries for 60 min and reperfusion was achieved for 24 h. Infarction volume in the ipsilateral hemisphere of ischemia/reperfusion animals was 114 .+-. 16 mm 3) in the 0.5% green tea pretreated animals compared to 181 .+-. 54 mm(3) in left hemisphere of nontreated animals. Green tea extract (0.5%) also reduced ischemia reperfusion-induced eicosanoid concentration: Leukotriene C(4) (from 245 .+-. 51 to186 .+-. 22), **prostoglandin** E(2) (from 306 .+-. 71 to 212 .+-. 43) and thromboxane A(2) (387 .+-. 69 to 251 .+-. 87 ng/mg protein). Ischemia/reperfusion-induced increases of hydrogen peroxide level (from 668 .+-. 76 to 801 .+-. 99 nmole/mg protein), lipid peroxidation products (from 1019 .+-. 112 to 630 .+-. 74 nmole/mg protein) and 8-oxodG formation (from 1.3 .+-. 0.3 to 0.5 .+-. 0.2 ng/mg DNA, x10(-2)) were also reduced. Moreover, 0.5% green tea extract also reduced the apoptotic cell number (from 44 .+-. 11 to 14 .+-. 1 in the striatum, and from 72 .+-. 11 to 42 .+-. 8 apoptotic cells/high power field in the cortex region). Green tea extract pretreatment also promoted recovery from the ischemia reperfusion-induced inhibition of active avoidance. The present study shows that the minimizing effect of green tea extract on the eicosanoid accumulation and **oxidative damage** in addition to the reduction of neuronal cell death could eventually result in protective effect on the ischemia/reperfusion-induced brain injury and behavior deficit. Copyright .COPYRGT. 2001 Elsevier Science Inc.
AU Hong C.T.; Ryu S.R.; Kim H.J.; Lee C.K.; Lee S.H.; Kim S.B.; Yun Y.P.; Ryu S.H.; Lee B.M.; Kim H.Y.
SO Brain Research Bulletin, (2001) 53/6 (743-749).
Refs: 27
ISSN: 0361-9230 CODEN: BRBUDT
TI Neuroprotective effect of green tea extract in experimental ischemia-reperfusion brain injury.

L10 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2001 ISI (R)
AB Eicosanoids accumulation and formation of oxygen free radicals have been implicated in the pathogenesis of ischemia reperfusion brain injury. In the present study, we examined whether green tea extract protects against ischemia/reperfusion-induced brain injury by minimizing eicosanoid accumulation and oxygen radical-induced **oxidative damage** in the brain. Green tea extract (0.5%) was orally administered to Wistar rats for 3 weeks before induction of ischemia. Ischemia was induced by the occlusion of middle cerebral arteries for 60 min and reperfusion was achieved for 24 h. Infarction volume in the ipsilateral hemisphere of ischemia reperfusion animals was 114 +/- 16 mm(3) in the 0.5% green tea pretreated animals compared to 181 +/- 54 mm(3) in left hemisphere of nontreated animals. Green tea extract (0.5%) also reduced ischemia reperfusion-induced eicosanoid concentration: Leukotriene C-4 (from 245 +/- 51 to186 +/- 22), **prostoglandin** E-2 (from 306 +/- 71 to 212 +/- 43) and thromboxane A(2) (387 +/- 69 to 251 +/- 87 ng/mg protein). Ischemia/reperfusion-induced increases of hydrogen peroxide

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level (from 688 +/- 76 to 501 +/- 99 nmole/mg protein), lipid peroxidation products (from 1013 +/- 110 to 820 +/- 70 nmole/mg protein) and 8-oxodG formation (from 1.3 +/- 0.3 to 0.8 +/- 1.2 ng/mug DNA, x10(-2)) were also reduced. Moreover, 0.5% green tea extract also reduced the apoptotic cell number (from 44 +/- 11 to 29 +/- 1 in the striatum, and from 72 +/- 11 to 41 +/- 5 apoptotic cells/high power field in the cortex region). Green tea extract pretreatment also promoted recovery from the ischemia/reperfusion-induced inhibition of active avoidance. The present study shows that the minimizing effect of green tea extract on the eicosanoid accumulation and **oxidative damage** in addition to the reduction of neuronal cell death could eventually result in protective effect on the ischemia/reperfusion-induced brain injury and behavior deficit. (C) 2001 Elsevier Science Inc.

AU Hong J T (Reprint); Ryu S Y; Kim H C; Lee J K; Lee S H; Kim D B; Yun Y P; Ryu J H; Lee B M; Kim P Y

SO BRAIN RESEARCH BULLETIN, (DEC 2001) Vol. 56, No. 6, pp. 743-749. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0361-9230.

TI Neuroprotective effect of green tea extract in experimental ischemia-reperfusion brain injury

=> d hist

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L1 119419 S (OXIDANT OR OXIDATIVE) (W) STRESS
L2 365 S (POLYMERIZE OR POLYMERIZED OR POLYMERIZATION) (W) (PEPTIDE OR
L3 1 S L1 AND L2

FILE 'REGISTRY' ENTERED AT 16:53:41 ON 28 AUG 2002
L4 1 S 37025-41-8/RN
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L5 1 S L1 AND (PROSTOGLANDIN OR CYCTOCHROME)
L6 137259 S (OXIDANT OR OXIDATIVE) (W) (STRESS OR DAMAGE)
L7 2 S L6 AND L2
L8 137259 S (OXIDANT OR OXIDATIVE) (W) (STRESS OR DAMAGE)
L9 1 S L8 AND L5
L10 4 S L8 AND (PROSTOGLANDIN OR CYCTOCHROME)

=> s l8 and l1
L11 2 L8 AND L1

=> d l11 all

L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
AN 2002:143229 CAPLUS
DN 136:130162
TI Assessment of **oxidant stress** in vitro and in vivo
IN Kim, Hyesook; Roberts-Kirchoff, Elizabeth Starr
PA USA
SO U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DT Patent

08/03/01

09921880

LA English
IC ICM C12Q001-26
ICS G01N033-53
NCL 435025000
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20020022244	A1	20020221	US 2001-915776	20010726
PRAI	US 2000-221631P	P	20000728		

AB There is provided a method of assessing **oxidant stress** by measuring polymn. of proteins. Also provided is a marker for **oxidant stress** which includes a **polymd. protein.** A kit for use in assessing **oxidant stress**, the kit including an assay for detecting **polymd. proteins** is also provided. A method of lowering **oxidant stress** by administering to a patient an effective amt. of at least one reducing agent is also provided. A pharmaceutical compn. for lowering **oxidant stress**, the pharmaceutical having an effective amt. of reducing agent and a pharmaceutically acceptable carrier is also provided.

ST **oxidant stress**

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Nitrated, polymd.; assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Polymd.; assessment of **oxidant stress** in vitro and in vivo)

IT Biomarkers (biological responses)
Composition
Distribution
Drugs
Nitration
Oxidation
Oxidative stress, biological
Oxidizing agents
Polymerization
Reducing agents
Reduction
Test kits
(assessment of **oxidant stress** in vitro and in vivo)

IT Dimers
RL: ANT (Analyte); ANST (Analytical study)
(assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(assessment of **oxidant stress** in vitro and in vivo)

IT Drug delivery systems
(carriers; assessment of **oxidant stress** in vitro and in vivo)

IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(disulfide bonded polymd.; assessment of **oxidant stress** in vitro and in vivo)

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IT Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(nitrated disulfide bonded polymd.; assessment of **oxidant stress** in vitro and in vivo)
IT 1903[illegible]-14-4, Peroxynitrite
RL: ANT (Analyte); ANST (Analytical study)
(assessment of **oxidant stress** in vitro and in vivo)
IT 9007-43-6D, Cytochrome c, nitrated, polymd. 27035-41-8, Oxidized glutathione 39391-19-9, Prostaglandin h2 synthase 39391-18-8D, Prostaglandin H2 synthase, nitrated, polymd.
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(assessment of **oxidant stress** in vitro and in vivo)
IT 39391-18-8D, Prostaglandin H2 synthase, nitrated dimer
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(assessment of **oxidant stress** in vitro and in vivo)
IT 70-18-8, Reduced glutathione, biological studies 9007-43-6, Cytochrome c, biological studies
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(assessment of **oxidant stress** in vitro and in vivo)
IT 1[illegible]-67-4, Peroxynitrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(assessment of **oxidant stress** in vitro and in vivo)

=> d l11 all 2

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1995:944469 CAPLUS
DN 124:7153
TI **Oxidative damage** of glycated protein
AU Cheng, Rong-zhu; Kawakishi, Shunro
CS Department Applied Biological Sciences, Nagoya University, Nagoya, Japan
SO Contributions to Nephrology (1995), 112(Dialysis-Related Amyloidosis), 11-17
CODEN: CNEPDD; ISSN: 0302-5144
PB Karger
DT Journal
LA English
CC 14-6 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 34
AB The authors investigated in detail the protein damages, esp. polymn., that arise by the action of glycated peptide, N.epsilon.-fructoselysine (FL), glucosone and cupric ion. Some of the results suggest that the polymn. may have arisen from a radical reaction that initiated in the glucosone/cupric ion/oxygen complex.
ST protein polymn cupric ion radical diabetes
IT Diabetes mellitus
Polymerization
(**protein** polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)
IT Reactive oxygen species
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(protein polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)
IT Glycoproteins, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM

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(Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(protein polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)
IT Rearrangement
(Amadori, protein polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)
IT 7782-44-7D, Oxygen, radicals
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)
IT 15158-11-9, Cupric ion, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)
IT 1854-26-7, D-Glucosone 31291-40-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein polymn. in relation to glycated peptide, N.epsilon.-fructoselysine, glucosone and cupric ion)

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FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 16:51:09 ON 28 AUG 2002
L1 119414 S (OXIDANT OR OXIDATIVE) (W) STRESS
L2 366 S (POLYMERIZE OR POLYMERIZED OR POLYMERIZATION) (W) (PEPTIDE OR
L3 1 S L1 AND L2

FILE 'REGISTRY' ENTERED AT 16:53:41 ON 28 AUG 2002
L4 1 S 27025-41-8/RN
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L5 1 S L1 AND (PROSTOGLANDIN OR CYCTOCHROME)
L6 137253 S (OXIDANT OR OXIDATIVE) (W) (STRESS OR DAMAGE)
L7 1 S L5 AND L2
L8 137253 S (OXIDANT OR OXIDATIVE) (W) (STRESS OR DAMAGE)
L9 1 S L8 AND L5
L10 4 S L8 AND (PROSTOGLANDIN OR CYCTOCHROME)
L11 2 S L8 AND L2

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NEWS 3	Apr 29	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 29	ZDB will be removed from STN
NEWS 5	Apr 29	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 29	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
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NEWS 8	Apr 30	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 3	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 12	PROMT no longer contains STANDARDS file segment
NEWS 13	Jul 17	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
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NEWS 18	Aug 8	NIOSHTIC has been reloaded and enhanced
NEWS 19	Aug 14	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 14	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 14	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28	Oct 01	EVENTLINE has been reloaded
NEWS 29	Oct 04	BEILSTEIN adds new search fields
NEWS 30	Oct 04	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002

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NEWS 32 Nov 18 DKILIT has been renamed APOLLIT

NEWS EXPRESS October 14 CURRENT WINDOWS VERSION IS V6.01,
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
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=> s (polymerization or polymerisation) (w) proteins
L1 15 (POLYMERIZATION OR POLYMERISATION) (W) PROTEINS

=> s (polymerization or polymerisation) and (stress or damage or oxidation or oxidize or oxidant)
L2 17435 (POLYMERIZATION OR POLYMERISATION) AND (STRESS OR DAMAGE OR OXIDATION OR OXIDIZE OR OXIDANT)

=> s l1 and (cytochrome (w) c)
L3 3 L1 AND (CYTOCHROME (W) C)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (15 DUPLICATES REMOVED)

=> s l4 and py<=2000
1 FILES SEARCHED...
4 FILES SEARCHED...
L5 28 L4 AND PY<=2000

=> d l5 1-28 py ti so au ab

L5 ANSWER 1 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
PY 2000
TI Cytoskeletal disruption accelerates caspase-3 activation and alters the intracellular membrane reorganization in DNA **damage**-induced apoptosis.

09/03/01

SO Experimental Cell Research, (**August 25, 2000**) Vol. 259, No. 1, pp. 64-78. print.
ISSN: 0014-4827.

AU Yamazaki, Yoshimitsu (1); Tsuruga, Mie; Zhou, Deshan; Fujita, Yasuko; Shang, Xueyuan; Tang, Yong; Kawasaki, Kazunori; Oka, Syuichi

AB In actinomycin D (AD)-induced apoptosis, caspase-3 activation and DNA cleavage in human megakaryo-blastic leukemia CMK-7 cells were greatly accelerated by tubulin and actin **polymerization** inhibitors (i.e., colcemid (CL) and cytochalasin D (CD), respectively), but the acceleration was not found with Taxol or phalloidin. A decrease in mitochondrial transmemorane potential, release of **cytochrome c** into the cytosol, and cleavage of procaspase-9 to its active form preceded the activation of caspase-3 and, moreover, all of these events began earlier and/or proceeded faster in cells treated with AD plus CL or CD than in cells treated with AD only. These results suggest that cytoskeletal disruption in the apoptotic cells promotes **damage** of the mitochondrial membrane, resulting in the enhanced release of **cytochrome c** necessary for the activation of caspase-9 that initiates the caspase cascade. On the other hand, apoptotic bodies were rapidly formed from cells treated with AD and CL, but were suppressed when treated with AD and CD. Intracellular membranes and the actin system were reorganized to surround the nuclear fragments in the AD-and CL-treated cells, but such a membrane system was not formed in the presence of CD, implying that the apoptotic bodies are formed via reorganization of intracellular membranes under regulation by actin **polymerization**. Thus, the cytoskeletal change in CMK-7 cells has a strong effect on the early biochemical process as well as on the later morphologic process in AD-induced apoptosis.

L5 ANSWER 2 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
PY 1998
TI Identification of o-phenylenediamine **polymerization** product catalyzed by **cytochrome c**.
SO Journal of Molecular Catalysis B Enzymatic, (**Jan. 2, 1998**) Vol. 4, No. 1-2, pp. 33-39.
ISSN: 1381-1177.

AU Zhu, Yimin; Li, Jinghong; Liu, Zhiming; Cheng, Guangjin; Dong, Shaojun (1); Wang, Erkang

AB The hydrogen peroxide (H_2O_2) and **cytochrome c** -dependent **oxidation** of o-phenylenediamine (o-PD) was investigated by spectrophotometry and electrochemistry. The results indicated that o-PD underwent facile catalytic **oxidation** in the presence of **cytochrome c**, and that the degradation of **cytochrome c** by hydrogen peroxide can also be partly prevented in the presence of o-PD. The hydroxyl radical scavengers (mannitol and sodium benzoate) and oxo-heme species scavenger (uric acid) do not inhibit the **oxidation**, which implies that the hydroxylation of o-PD may not be involved in its **oxidation**. Combining with the results of the mass spectrum, elemental analysis, nuclear magnetic resonance and Fourier transform infrared spectrum of the isolated product, a conceivable structure of the product was suggested.

L5 ANSWER 3 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
PY 1997
TI Ca-2+-independent permeabilization of the inner mitochondrial membrane by peroxynitrite is mediated by membrane protein thiol cross-linking and lipid peroxidation.
SO Archives of Biochemistry and Biophysics, (1997) Vol. 345, No. 2, pp. 243-250.
ISSN: 0003-9861.

AU Sadeiha, F. R. (1); Thomson, L.; Fagian, M. M.; Costa, A. D. T.; Radi, R.;

09921880

Verbesi, A. E.

AB Peroxynitrite anion, the reaction product of superoxide and nitric oxide, is a potent biological **oxidant**, which inactivates mammalian heart mitochondrial NADH-coenzyme Q reductase (complex I), succinate dehydrogenase (complex II), and ATPase, without affecting **cytochrome c** oxidase (complex IV). In this paper, we evaluated the effect of peroxynitrite on mitochondrial membrane integrity and permeability under low calcium concentration. Phosphate buffer was used in most of our experiments since Hepes, Tris, mannitol, and sucrose were found to inhibit the oxidative chemistry of peroxynitrite. Peroxynitrite (0.1-1.0 mM) caused a dose-dependent decrease in the ability of mitochondria to build up a membrane potential when N,N,N',N'-tetramethyl-p-phenylenediamine/ascorbate were used as substrate. Elimination of the membrane potential was accompanied by penetration of the osmotic support (KCl/NaCl) into the matrix as judged by the parallel occurrence of mitochondrial swelling. This swelling was partially inhibited by dithiothreitol (DTT) or butylated hydroxytoluene (BHT) and was insensitive to ethylene glycol-bis(beta-aminoethyl ether)N,N,N',N'-tetraacetic acid, ADP, and cyclosporin A. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of solubilized membrane proteins indicated that alterations in membrane permeability were associated with the production of protein aggregates due to membrane protein thiol cross-linking. The protective effect of DTT on both mitochondrial swelling and protein **polymerization** suggests the involvement of disulfide bonds in the membrane permeabilization process. In addition, the increase in thiobarbituric acid-reactive substances and the partial inhibitory effect of BHT indicate the occurrence of lipid peroxidation. These results support the idea that under our experimental conditions peroxynitrite causes mitochondrial structural and functional alterations by Ca-2+-independent mechanisms through lipid peroxidation and protein sulfhydryl **oxidation.**

L5 ANSWER 4 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
PY 1987
TI TYROSINASE CATALYZED PROTEIN **POLYMERIZATION** AS AN IN-VITRO MODEL FOR QUINONE TANNING OF INSECT CUTICLE.
SO ARCH INSECT BIOCHEM PHYSIOL, (1987) 4 (1 , 9-26.
CODEN: AIBPEA. ISSN: 0739-4462.
AU SUGUMARAN M; HERRIDGAN B; O'BRIEN J
AB The validity of Pryor's widely accepted quinone tanning hypothesis for the sclerotization of insect cuticle was examined using an in vitro model system. Quinones generated in situ by the **oxidation** of catechols with mushroom tyrosinase and molecular oxygen readily reacted with test proteins such as lysozyme, ribonuclease and **cytochrome-c** , producing dimers, trimers, and higher oligomers. With the exception of 3,4-dihydroxyphenylalanine, dopamine, and norepinephrine, most other catechols tested participated in protein **polymerization.** The inability of these three compounds to support oligomerization of test protein was attributed to their high rate of intramolecular cyclization reaction. Radioactive incorporation studies reveal the formation of catechol-protein adducts, as well as aryl-protein crosslinks in the reaction mixture. The above results strongly support the quinone tanning hypothesis. Based on these findings, the mechanism of cuticular sclerotization is discussed.

L5 ANSWER 5 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
PY 1985
TI THE PURIFICATION AND PROPERTIES OF CELLOBIOSE DEHYDROGENASE FROM SCLEROTIUM-ROLFSII AND ITS ROLE IN CELLULOLYSIS.
SO J GEN MICROBIOL, (1985) 131 (8), 1917-1924.
CODEN: JGMIAN. ISSN: 0022-1287.

08/03/01

09921890

AU SAISAVA J C; PATIL R V
AB An extracellular cellobiose dehydrogenase was purified from the culture filtrates of S. rolfsii. The purified enzyme is homogeneous as determined by disc gel electrophoresis, with and without sodium dodecyl sulfate, and by analytical isoelectric focusing in polyacrylamide gel. The enzyme is a single-subunit glycoprotein containing 5.9% total carbohydrate; its MW is 63,000-64,500, and its isoelectric point, 5.1. The enzyme oxidized cellobiose, other cellodextrins and lactose whereas other disaccharides tested were not utilized as substrates. The rate of cellodextrin **oxidation** decreased and the Km increased with increasing degree of **polymerization** of the substrate. **Cytochrome c** was reduced though at a considerably lower rate than 2,6-dichlorophenolindophenol. The natural electron acceptor for the enzyme was identified.

L5 ANSWER 6 OF 28 MEDLINE
PY 1993
TI Spin trapping of superoxide radicals following stimulation of neutrophils with fMLP is temperature dependent.
SO FREE RADICAL BIOLOGY AND MEDICINE, **(1993 Oct)** 15 (4) 423-33.
Journal code: 8709159. ISSN: 0891-5849.
AU Taniguwa T; Kotake Y; Reinke L A
AB Oxygen radical formation by human neutrophils stimulated with a chemotactic peptide, formyl-methionyl-leucyl-phenylalanine (fMLP), was studied through the use of spin trapping and superoxide dismutase-inhibitable reduction of oxidized **cytochrome c**. Both methods provided comparable data on temperature-dependent kinetics of superoxide radical formation, but hydroxyl radicals were also detected in spin-trapping experiments. When superoxide generation was monitored at 37 degrees C, the respiratory burst lasted only a few minutes. If the neutrophils were stimulated at 37 degrees C, but superoxide measurements were done at room temperature, the respiratory burst was again transient. However, neutrophils persistently generated superoxide when both stimulation and subsequent measurements were performed at room temperature. In the presence of the actin **polymerization** inhibitor, cytochalasin B, superoxide generation was persistent, even when measurements were conducted at 37 degrees C. A possible explanation for these observations is that the fMLP receptor complexes quickly aggregate and are internalized at physiological temperature, but not at room temperature. Very little superoxide was formed if cells were kept at a temperature of 4 degrees C for 1 h prior to fMLP addition, which is consistent with decreased expression of the fMLP receptor at cold temperatures.

L5 ANSWER 7 OF 28 MEDLINE
PY 1990
TI Heterogeneous electron transfer of **cytochrome c** facilitated by polypyrrole and methylene blue polypyrrole film modified electrodes.
SO JOURNAL OF INORGANIC BIOCHEMISTRY, **(1990 Nov)** 41 (3) 189-95.
Journal code: 7905788. ISSN: 0162-0134.
AU Zhang W B; Song S H; Dong S J
AB Polypyrrole and methylene blue incorporated polypyrrole thin-film modified electrodes were prepared by the electrochemical **polymerization** method. These modified electrodes may facilitate heterogeneous electron transfer of **cytochrome c** with high electrocatalytic activity and good stability. Optical thin-layer spectroelectrochemical techniques were used to determine the characteristics of these electrochemical processes such as formal redox potential (E0), electron transfer number (n), and the apparent rate constant (ks.h0).

09/13/01

L5 ANSWER 8 OF 25 MEDLINE
PY 1983
TI Studies on the ferricytochrome a-ferrocytochrome a3-carbon monoxide complex of mammalian cytochrome oxidase. Conditions for preparation and some properties.
SO JOURNAL OF BIOCHEMISTRY, **(1983 Apr)** 93 (4) 997-1010.
Journal code: 0376600. ISSN: 0021-924X.
AU Horie S; Watanabe T; Ave K
AB The conditions for the preparation of the ferricytochrome a-ferrocytochrome a3-carbon monoxide complex (a3+, a3(2)+CO) of cytochrome oxidase [EC 1.9.3.1] by the ferricyanide-reoxidation method and some properties of the prepared complex were studied. The addition of a small volume of concentrated ferricyanide solution to the dithionite-reduced and carbon monoxide-treated cytochrome oxidase preparation was required to obtain the (a3+, a3(2)+CO) spectrum showing absorption maxima at 590, 545, and 423 nm. The addition of larger volumes of ferricyanide solution, thus introducing larger amounts of oxygen into the preparation, caused decomposition of the carbon monoxide complex. A part of the added ferricyanide was immediately reduced by dithionite whereas the remainder was gradually reduced by partial **oxidation** product(s) of dithionite. The (a3+, a3(2)+CO) complex was stable only when excess ferricyanide remained in the reaction mixture. The formation of the (a3+, a3(2)+CO) spectrum was observed when sodium citrate, phosphate or borate buffer containing either cholate or a non-ionic detergent was employed as the solvent buffer, but not with the buffers containing sodium dodecyl sulfate (SDS) or cetyltrimethyl-ammonium bromide (CETAB). The formation was considerably inhibited by trishydroxymethyl-aminomethane(Tris)-HCl buffer. The (a3+, a3(2)+CO) spectrum appeared with maximal intensity at around pH 7. The pH-dependency of the intensity of the spectrum was not in parallel with the pH-dependent change of the **polymerization** state of the cytochrome oxidase preparation. On freezing to liquid nitrogen temperature, the (a3+, a3(2)+CO) complex prepared in usual solvent buffers was mostly converted to the oxidized form of cytochrome oxidase (a3+, a3(2)+. However, when prepared in the phosphate buffer, pH 8.0, containing 1.2% (w/v) sodium cholate and with 20% saturation with ammonium sulfate, the complex mostly remained unchanged after the freezing. Based on the results obtained, the stability of the juxta-heme structure of cytochrome a3 was also discussed.

L5 ANSWER 9 OF 25 CABLUS COPYRIGHT 2002 ACS
PY **2000**
TI Sodium azide induces **damage** of microtubules and cell viability in cultured nerve cells
SO Zhongguo Shenjing Kexue Zazhi (**2000**), 16(3), 267-269
CODEN: ZSKZFN
AU Zhang, Lan; Li, Lin; Liu, Shi-sen; An, Wen-Lin; Xue, Bing; Ban, Li-Qin; Li, Xiao-Ming; Xu, Yan-Ling
AB We have investigated the effects of sodium azide, a specific inhibitor of **cytochrome c** oxidase (COX), on the microtubule morphol. and cell viability of nerve cells. Human neuroblastoma SH-SY5Y cells were exposed to sodium azide to check mitochondrial complex IV activity by microassay method, cell viability by MTT method and microtubules by confocal microscopy and image analyzer. Exposed to 16-64 mmol/L sodium azide for 1 h, the mitochondrial complex IV activity decreased dose-dependently. MTT assay showed a dose- and time-dependent decrease of cultured nerve cells which were treated with 16-128 mmol/L sodium azide for 1-8 h. Exposed to 64 mmol/L sodium azide for 4 h, the processes of cells were shortened, almost disappeared, cell bodies became round and bright under contrast microscope. Meanwhile, microtubules were disassembled and became disorderly, the content and distribution of tubulin (microtubule protein) were reduced, especially in the processes.

It is indicated that sodium azide inhibits the assembly and **polymn**. of tubulin in microtubules. The **damage** of axons induced by microtubule collapse further blocks the intercellular signal transduction and intracellular material transportation which are essential to a cell.

L5 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY 1999
1999
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1999
TI Enzymic **oxidation** and modification of substrates
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
IN Hilding, Hindrik Jan; Van Dijk, Cees; Boeriu, Carmen Gabriela
AB An enzymic **oxidn.** process comprises bringing together an oxidative enzyme, a H acceptor, and a H donor in a reaction mixt. and causing an oxidative reaction to proceed under the influence of the enzyme with at least the H acceptor and the H donor as substrates, wherein a substrate for crosslinking is optionally further present in the reaction mixt. and the H donor serves as crosslinking agent. The H donor may be converted by the oxidative enzyme into a radical which subsequently serves as initiator in the **polymn.** of monomers also present in the reaction mixt., in particular acrylates. Alternatively, the H donor is an org. dye mol. which is linked by the oxidative enzymic reaction to another org. dye mols. Thus, ovalbumin was crosslinked by incubation with peroxidase, H2O2, and catechol to improve its foaming properties for use in foods.

L5 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1998**
TI Cellobiose dehydrogenase. Possible roles and importance for pulp and paper biotechnology
SO Bioresource Technology (**1998**), Volume Date 1999, 67(1), 43-46
CODEN: BIRTEB; ISSN: 0960-8524
AU Duarte, J. C.; Costa-Ferreira, M.; Sena-Martins, G.
AB A review with many refs. The FAD/heme enzyme cellobiose dehydrogenase (CDH) has been frequently isolated from several white-rot fungi, but is also produced by a few brown-rot fungi. CDH is a sugar oxidase that **oxidizes** cellobiose to cellobiono-1,5-lactone and reduces a great no. of electron acceptors such as quinones, phenoxy and cation radicals, Fe(III), **cytochrome c** and mol. oxygen. We suggest that CDH is involved in lignin degrdn. as this enzyme can reduce phenoxy radicals, and thereby regulate lignin **polymn.**/depolymn. Furthermore, we have shown that P. chrysosporium can produce CDH together with MnP and LiP, under conditions where lignin degrdn., measured as [14C] DHP mineralization, occurs and demonstrated how active CDH may help complete the catalytic cycles of the peroxidases when their natural substrates are not available. Possible physiol. roles of CDH on the mechanisms of lignin degrdn. and its potential for pulp and paper biotechnol. are presented.

L5 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1996**
TI Tailored Polymers To Probe the Nature of the Bioelectrochemical Interface
SO Langmuir (**1996**), 12(23), 5681-5688
CODEN: LANGD5; ISSN: 0743-7463
AU Ryden, K. S.; Morris, D. G.; Cooper, J. M.
AB A range of pyrrole monomers with carboxyl derivs. both at the N-, and meta.-ring positions were synthesized and, subsequently, were polymd. electrochem. at carbon, gold, and platinum electrodes. The resulting polymers, which were characterized with both electrochem. and

spectroscopic methods, were then used to investigate the importance of polymer **oxidn.** potential, polymer functionality, and backbone cond. on the redox interaction with the small redox protein, **cytochrome c**. By choosing monomer substituents with varying side-chain length and steric bulk, it was possible to probe the nature of the protein-polymer interaction and to show how the heterogeneous rate consts., ks, as an est. for electron exchange between the electrode functionalized poly(pyrroles) and the protein, varied as a consequence of the structure of the matrix. The method provides a novel route for the modification of a wide range of conducting surfaces for the study of biol. interfacial reactions, particularly those involving biomol. recognition.

L5 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1993**
TI Characterization of polypyrrole films electrodeposited by water solutions: effect of the supporting electrolyte and **cytochrome c** immobilization
SO Electrochimica Acta (**1993**), 38(17), 2561-8
CODEN: ELCAAV; ISSN: 0013-4686
AU Agostiano, A.; Daselli, M.; DellaMonica, M.; Laera, S.
AB Modified electrodes were obtained by electrodeposition on Pt of polypyrrole (PP) from aq. solns. The electrodes obtained in the absence of **cytochrome c** were tested by cyclic voltammetry in aq. solns. contg. different supporting electrolytes. The current corresponding to the **oxidn.** and redn. of PP as well as the peak potentials depends, when using salts of the same cation, on the nature of the anion. The differences were interpreted in terms of the anion flux in and out the film and/or its adsorption on the film surface which accompanies the **oxidn.** and the redn. of the PP, resp. The change of the cation also produces some effect on the electrochem. film behavior. The modified film behaves like a metallic electrode, as it produces the cv of electroactive species in the soln., when the PP is in the oxidized form. If the electrode is exposed to very pos. potentials it cannot be reduced further, but shows selectivity as only some mols. can be reduced or oxidized. In the presence of incorporated **cytochrome c**, 2 new, well defined, **oxidn.** and redn. peaks are visible in cv. The peaks became more and more evident after successive cyclic scans.

L5 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY 1993
1993
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2001
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1993
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1993
TI Nonaqueous naphthalimide dyes, their preparation, and their uses
SO U.S., 16 pp.
CODEN: USXXAM
IN Lewis, David E.; Ubent, Ronald E.; Judy, Millard M.; Matthews, J. Lester
AB Predominantly hydrophobic nonaqueous N-substituted 1,8-naphthalimide compds. I (R, R' = straight-chain or branched C1-30 alkyl, etc.; X = F, Cl, Br, I) are disclosed, each bearing a nucleofuge at its 3-position and a heteroat. electron-releasing group at its 4-position. The heteroat. releasing group has a heteroatom directly linked to the 4-position of the ring and has .gtoreq.1 H directly attached to the heteroatom. The dyes of the invention can be monomeric or dimeric. On activation with an activating

agent (light energy, etc.) in an environment independent of the presence or absence of oxygen, these compds. generate activated species. The activated species initiate chem. changes in lipid bilayer membranes of viruses and other target cells which can eradicate the viruses or other target cells. The activated species can also cause structural changes in lipid and any assocd. proteins and polypeptides at a level beneath the surface of the membrane, leading to **polymn.** and crosslinking. Prepn. of selected I is described. Kinetic consts. for binding of I (R = R' = n-C6H13; X = Br) (II) (prepn. given) in synthetic vesicles of .beta.-oleyl-.gamma.-stearoylphosphatidylcholine and bleaching of II in the vesicles were detd. In studies with H9 cells and DAUDI cells, II was shown to be a potent mediator of photochem. toxicity and a highly efficient photochem. cell inactivator at concns. as low as 1 .mu.M and using light energy fluxes in the range of 10 J/cm2. Effect of monomeric and dimeric compds. on viruses, protein crosslinking, etc. are also reported.

L5 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY 1990
1992
1991
1990
TI Redox **polymerization** diagnostic test composition and method for immunoassay and nucleic acid hybridization assay
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
IN Oster, Gerald; Davis, Baruch C.
AB A diagnostic test compn. for detecting and measuring an analyte possessing biol. activity comprises (a) a redox catalyst system capable of converting a monomer to a polymer, the monomer capable of undergoing addn. **polymn.**, the redox catalyst system comprising .gtoreq.1 chem. moieties with 1) the analyte comprising .gtoreq.1 such moiety or 2) in the case that the analyte lacks a redox catalyst property, the analyte is linked by a specific ligand to .gtoreq.1 such moiety or is linked by the specific ligand to a generator of .gtoreq.1 such moiety; and; (b) .gtoreq.1 monomer capable of undergoing addn. **polymn.** Immunoassays and nucleic acid hybridization assays using redox **polymn.** are described. Thus, glucose oxidase coupled to antibody is reacted with an immobilized antigen spot on a glass slide, uncombined conjugate is washed off, and the slide is dipped into a soln. contg. Ca acrylate 1%, glucose 5%, and ascorbate acid 3.5% for 10 min to form a grossly visible white ppt. at the site of the antigen.

L5 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1969**
TI Influence of phospholipid peroxidation on the formation and properties of their complexes with **cytochrome c**
SO Rev. Roum. Biochim. (**1969**), 6(2), 111-16
CODEN: RRBCAD
AU Dinescu, Gabriela
AB Complexes of **cytochrome c** were prepd. with phospholipids in various stages of peroxidn. Lipids were extd. from normal rat tissue (brain, liver, kidney) and tumors (Jensen sarcoma, Guerin carcinoma). The influence of phospholipid peroxidn. on certain properties of the **cytochrome c** in complexes was studied, namely: peroxidase activity, stability to H2O2 action, and activity in cytochrome oxidase function. Lipoperoxides induced an advanced inactivation of the enzyme in complexes, due probably to **cytochrome c polymn.** The data are discussed in relation to the function of **cytochrome c** -phospholipid complexes in mitochondria, and the significance of their

damage due to lipoperoxides occurring in tissues, generally after irradn.

L5 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1967**
TI Antimycin-sensitive cleavage of complex III of the mitochondrial respiratory chain
SO J. Biol. Chem. (**1967**), 242(21), 4954-66
CODEN: JBCHA3
AU Riesbo, John S.; Baum, Harold; Stoner, Clinton D.; Lipton, Samuel H.
AB Complex III of the mitochondrial respiratory chain is cleaved either by bile salts in conjunction with (NH4)2SO4 or by low concns. of guanidinium salts, to yield an insol. fraction contg. cytochrome b and a sol. fraction contg. cytochrome c1. This cleavage is blocked absolutely by pretreatment of Complex III with antimycin A in an amt. stoichiometric with the **cytochrome c** content of the complex. However, under selected conditions (i.e. 0.1M guanidine-HCl or 0.2M guanidine-HCl plus freezing), guanidine cleaves Complex III despite pretreatment of the complex with antimycin A. Urea (4M) and methyl-substituted guanidines, as well as biguanide, are all relatively ineffective as promoters of the cleavage reaction; however, prolonged treatment of Complex III with low concns. of octylguanidine or phenylethylbiguanide is partially effective in cleaving the complex. Cleavage of Complex III appears to occur in 2 distinct steps: a primary, first-order destruction of sensitivity of cleavage to antimycin A, and a secondary step involving an antimycin-insensitive **polymerization** and pptn. of cytochrome b. The primary (antimycin-sensitive) process is accelerated at either acid or alk. pH values whether promoted by bile salt plus (NH4)2SO4 or by guanidine. The antimycin-sensitive cleavage is inhibited not only by antimycin A, but also by both 2-n-heptyl-4-hydroxyquinoline N-oxide and the antimycin analog, N-octadecyl-3-formamidosalicylamide. Redn. of Complex II, either by reducing substrates (succinate or reduced coenzyme Q) or by strictly chem. reagents (Na dithionite), mimics the action of antimycin A in causing a blockage of the cleavage reaction. Because this blockage cannot be ascribed to redn. of any of the characterized components of Complex III, it is proposed that a new **oxidn**.-redn. component with a potential intermediate between the potentials of cytochromes b and c1 is involved intimately with the site of cleavage and the antimycinsensitive site of Complex III. 39 references.

L5 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1966**
TI Effects of hydrogen peroxide on **cytochrome c**
SO Biochem. J. (**1966**), 101(3), 689
AU O'Brien, P. J.
AB Treatment of ferricytochrome c (I) with H2O2 at pH 7-10 decreased the .alpha., .beta., and Soret absorption bands in proportion to the concn. of H2O2. At pH 7 at room temp., 15 moles H2O2 per mole I decreased the bands by 50 %. Treatment with H2O2 decreased the ability of I to restore succinate **oxidn**. in extd. mitochondria. The decrease was greater than the decrease in the absorption bands, and redn. by NADH2: **cytochrome c** oxidoreductase, ascorbic acid, or cysteine was more difficult. The inhibition of the rate of redn. of I treated with H2O2 showed no pH dependence indicating that **polymerization** does not account for the effects of H2O2. Amino acid analysis of I after treatment with H2O2 showed that tyrosine had been destroyed.

L5 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2002 ACS
PY **1961**
TI Radiation **damage** to proteins
SO Nature (**1961**), 191, 1304-5

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AU Mumta, U. S.; Tappel, A. L.
AB One-tenth percent solns. of **cytochrome c**, hemoglobin, catalase, and egg albumin were anaerobically exposed to 0.6-2 m.e.v. gamma.-irradiation in a dose from 105 to 5 .times. 10^7 rads. Amino acid analyses were made on the insol. fraction, the Cl3CCO2H ppt., and the sol. scission products. Loss of biol. properties was not attributed to any specific loci. Results suggested that denaturation or **polymerization** was not the only cause for formation of insol. protein, and that radiation-induced hydrolysis was not the mechanism for fragmentation.

L5 ANSWER 20 OF 28 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
PY **1999**
TI Identification of o-phenylenediamine **polymerization** product catalyzed by **cytochrome c**.
SO Journal of Molecular Catalysis - B Enzymatic, (1999) 4/1-3 (33-39). Refs: 19
ISSN: 1381-1177 CODEN: JMCEF8
AU Chu Y.; Li J.; Liu Z.; Cheng G.; Dong S.; Wang E.
AB The hydrogen peroxide (H_2O_2) and **cytochrome c** -dependent **oxidation** of o-phenylenediamine (o-PD) was investigated by spectrophotometry and electrochemistry. The results indicated that o-PD underwent facile catalytic **oxidation** in the presence of **cytochrome c**, and that the degradation of **cytochrome c** by hydrogen peroxide can also be partly prevented in the presence of o-PD. The hydroxyl radical scavengers (mannitol and sodium benzoate) and oxo-heme species scavenger (uric acid) do not inhibit the **oxidation**, which implies that the hydroxylation of o-PD may not be involved in its **oxidation**. Combining with the results of the mass spectrum, elemental analysis, nuclear magnetic resonance and Fourier transform infrared spectrum of the isolated product, a conceivable structure of the product was suggested.

L5 ANSWER 21 OF 28 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
PY **1996**
TI Mechanism of simultaneous iodination and coupling catalyzed by thyroid peroxidase.
SO Archives of Biochemistry and Biophysics, (1996) 330/1 (24-32).
ISSN: 0003-9861 CODEN: ABBIA4
AU Taurog A.; Dorris M.L.; Doerge D.R.
AB Thyroid peroxidase (TPO) simultaneously catalyzes two very different types of reaction in the thyroid gland-iodination and coupling. The present study addresses the mechanism of this simultaneous dual activity. Compound I, the two-electron **oxidation** product of TPO, exists in two different forms-an oxoferryl porphyrin .pi.-cation radical and an oxoferryl protein radical. It has been proposed that iodination is mediated by the porphyrin .pi.-cation radical form of TPO compound I, while coupling is mediated by the protein radical form. However, results obtained in the present study favor the view that both iodination and coupling are mediated by the porphyrin .pi.-cation radical form of compound I. In the first part of the study, we compared coupling and iodination activities of two peroxidases with very similar crystal structures-**cytochrome c** peroxidase (CcP) and lignin peroxidase (LiP). Although these two peroxidases have very similar three-dimensional structures, CcP forms a compound I only of the protein radical type, whereas compound I of LiP exists only as a porphyrin .pi.-cation radical. Comparison of the catalytic activities of the two enzymes showed that diiodotyrosine (DIT)- stimulated coupling activity of LiP was significantly greater than that of CcP. Moreover, lignin peroxidase displayed very significant iodinating activity at acid pHs, whereas iodination with CcP was negligible at all pHs tested. Our

findings with these two structurally similar peroxidases suggested that TPO-catalyzed iodination and coupling could both be mediated by the porphyrin .pi.-cation radical form of compound I. More direct evidence in support of this view was obtained in the second part of this study, employing TPO and lactoperoxidase (LPO) model systems in which iodination and coupling occurred simultaneously. Heme spectral analysis was used to correlate formation of the protein radical form of compound I with the kinetics of the iodination and coupling reactions. Formation of the compound I protein radical was not observed until the iodination and coupling reactions had almost been completed. In separate experiments it was shown that the spontaneous conversion of the porphyrin .pi.-cation radical form of TPO or LPO compound I to the protein radical form was markedly inhibited by a low concentration of iodide, especially in the presence of an iodide acceptor. These studies provide compelling evidence that both iodination and coupling are mediated by the porphyrin .pi.-cation radical form of compound I. This was further substantiated by the finding that coupling was inhibited in the presence of excess iodide, an observation readily explained by competition between iodide and DIT residues in thyroglobulin for **oxidation** by the porphyrin .pi.-cation radical.

L5 ANSWER 12 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
PY **1994**
TI Microbially mediated formation of benzonaphthothiophenes from benzo[b]thiophenes.
SO Applied and Environmental Microbiology, (1994) 60/10 (3634-3638). ISSN: 0099-2240 CODEN: AEMIDF
AU Kropp K.G.; Gonzalves J.A.; Andersson J.T.; Fedorak P.M.
AB Studies of the microbial metabolism of benzo[b]thiophene (molecular weight 134) by three Pseudomonas isolates showed the formation of benzothiophene sulfoxide, benzothiophene sulfone, and a sulfur-containing metabolite with a molecular weight of 234. Desulfurization of the high-molecular-weight product with nickel boride gave 1-phenylnaphthalene, indicating that the metabolite was benzo[b]naphtho[1,2-d]thiophene. Similarly, the isolates were capable of producing the analogous dimethyl-substituted benzonaphthothiophenes from methylbenzothiophenes that had the methyl substitution on the benzene ring. The formation of benzo[b]naphtho[1,2-d]thiophene was also observed when a petroleum-degrading mixed culture was incubated with benzothiophene- supplemented Prudhoe Bay crude oil. Investigations into the mechanism of formation of these high-molecular-weight compounds showed that they resulted from an abiotic, Diels-Alder-type condensation of two molecules of the sulfoxide, which were microbially produced from the respective benzothiophene, with the subsequent loss of two atoms of hydrogen and one atom of sulfur. The condensation products also formed from the sulfoxides of benzothiophene and methylbenzothiophenes when the sulfoxides were enzymatically synthesized by **oxidation** of the benzothiophene with horse heart **cytochrome c** and H2O2.

L5 ANSWER 13 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2000
TI Arabidopsis ATP A2 peroxidase. Expression and high-resolution structure of a plant peroxidase with implications for lignification
SO PLANT MOLECULAR BIOLOGY, (**SEP 2000**) Vol. 44, No. 2, pp. 231-249. Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS. ISSN: 0167-4412.
AU Ostergaard L; Teilum K; Mirza O; Mattsson O; Petersen M; Welinder K G; Mundy J; Gajhede M; Henriksen A (Reprint)
AB Lignins are phenolic biopolymers synthesized by terrestrial, vascular plants for mechanical support and in response to pathogen attack.

09921880

Peroxidases have been proposed to catalyse the dehydrogenative **polymerization** of monolignols into lignins, although no specific isoenzyme has been shown to be involved in lignin biosynthesis. Recently we isolated an extracellular anionic peroxidase, ATP A2, from rapidly lignifying Arabidopsis cell suspension culture and cloned its cDNA. Here we show that the Atp A2 promoter directs GUS reporter gene expression in lignified tissues of transgenic plants. Moreover, an Arabidopsis mutant with increased lignin levels compared to wild type shows increased levels of ATP A2 mRNA and of a mRNA encoding an enzyme upstream in the lignin biosynthetic pathway. The substrate specificity of ATP A2 was analysed by X-ray crystallography and docking of lignin precursors. The structure of ATP A2 was solved to 1.45 Angstrom resolution at 11° K. Docking of p-coumaryl, coniferyl and sinapyl alcohol in the substrate binding site of ATP A2 were analysed on the basis of the crystal structure of a horseradish peroxidase C-CN-ferulic acid complex. The analysis indicates that the precursors p-coumaryl and coniferyl alcohols are preferred by ATP A2, while the **oxidation** of sinapyl alcohol will be sterically hindered in ATP A2 as well as in all other plant peroxidases due to an overlap with the conserved Pro-139. We suggest ATP A2 is involved in a complex regulation of the covalent cross-linking in the plant cell wall.

L5 ANSWER 24 OF 29 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2000
TI Differential regulation of HSP27 oligomerization in tumor cells grown in vitro and in vivo
SO ONCOGENE, (**5 OCT 2000**) Vol. 19, No. 42, pp. 4855-4867.
Publisher: NATURE PUBLISHING GROUP, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 0950-9232.
AU Bruey J M; Paul C; Thomenin A; Hilpert S; Arrigo A P; Solary E; Garrido C
Reprint
AB HSP27 form oligomeric structures up to 800 Kda. In cultured cells, the equilibrium between small and large oligomers shifted towards smaller oligomers when phosphorylated on serine residues. To further explore HSP27 structural organization and its repercussion in HSP27 antiapoptotic and tumorigenic properties, we transfected colon cancer HEG cells with wild type HSP27 and two mutants in which the phosphorylatable serine residues have been replaced by alanine (to mimic the non phosphorylated protein) or aspartate (to mimic the phosphorylated protein). In growing cells, wild type and alanine mutant formed small and large oligomers and demonstrated antiapoptotic activity while aspartate mutant only formed small multimers and had no antiapoptotic activity. In a cell-free system, only large oligomeric structures interfered with **cytochrome c** -induced caspase activation, thereby inhibiting apoptosis. The inability of the aspartate mutant to form large oligomers and to protect tumor cells from apoptosis was overcome by growing the cells in vivo, either in syngenic animals or nude mice. These observations were reproduced by culturing the cells at confluence in vitro. In conclusion (1) large oligomers are the structural organization of HSP27 required for its antiapoptotic activity and (2) cell-cell contacts induce the formation of large oligomers, whatever the status of phosphorylatable serines, thereby increasing cell tumorigenicity.

L5 ANSWER 25 OF 29 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2000
TI The latest progress on electron transfer in macromolecule-metal complexes and future scope of MMC
SO MACROMOLECULAR SYMPOSIA, (**JUL 2000**) Vol. 156, pp. 1-9.
Publisher: WILEY-V C H VERLAG GMBH, MUHLENSTRASSE 33-34, D-13187 BERLIN, GERMANY.
ISSN: 1022-1360.

09/683,681

AU Tsuchida E (Reprint)
AB We have been developing a method to regulate the electronic processes of the O-2-coordinated metal complexes using macromolecules, including synthetic polymers, molecular assemblies, and multi-nuclear complexes. Acceleration of the electron transfer leads a variety of molecular conversions. Mixed valent vanadyl complexes, for example, act as a multi-electron transfer mediator for the oxidative **polymerization** of the diphenyl disulfide, and a pure and high molecular weight poly(thiophenylene) can be obtained. At the same time, the dinuclear vanadium complex acts as an efficient catalyst for the four-electron reduction of dioxygen to water. We have recently expanded this reaction to other mu-oxo dimeric complexes. On the other hand, prevention of the electron transfer process increases the stability of the O-2-adduct compounds. The tetraphenylporphyrinato-iron(II) derivative incorporated into human serum albumin can reversibly bind and release dioxygen under physiological conditions (in aqueous media, pH 7.4, 37 degrees C) like hemoglobin and myoglobin. The microenvironment around the porphyrinatoiron in the albumin structure retards the irreversible **oxidation** of the central iron(II). The O-2-binding ability of this synthetic hemoprotein satisfies the clinical requirements for O-2-infusion as a red blood cell substitute.

L5 ANSWER 27 OF 28 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2000
TI Superoxide dismutase as a target for the selective killing of cancer cells
SO NATURE, (**21 SEP 2000**) Vol. 407, No. 6802, pp. 390-395.
Publisher: MACMILLAN PUBLISHERS LTD, PORTERS SOUTH, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
ISSN: 0028-0836.
AU Huang P (Reprint); Feng L; Oldham E A; Keating M J; Plunkett W
AB Superoxide dismutases (SOD) are essential enzymes that eliminate superoxide radical (O-2(-)) and thus protect cells from **damage** induced by free radicals(1-3). The active O-2(-) production and low SOD activity in cancer cells(3-7) may render the malignant cells highly dependent on SOD for survival and sensitive to inhibition of SOD. Here we report that certain oestrogen derivatives selectively kill human leukaemia cells but not normal lymphocytes. Using complementary DNA microarray and biochemical approaches, we identify SOD as a target of this drug action and show that chemical modifications at the 2-carbon (2-OH, 2-OCH3) of the derivatives are essential for SOD inhibition and for apoptosis induction. Inhibition of SOD causes accumulation of cellular O-2(-) and leads to free-radical-mediated **damage** to mitochondrial membranes, the release of **cytochrome c** from mitochondria and apoptosis of the cancer cells. Our results indicate that targeting SOD may be a promising approach to the selective killing of cancer cells, and that mechanism-based combinations of SOD inhibitors with free-radical-producing agents may have clinical applications.

L5 ANSWER 28 OF 28 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 1999
TI A photodynamic pathway to apoptosis and necrosis induced by dimethyl tetrahydroxyanthrone and hypericin in leukaemic cells: possible relevance to photodynamic therapy
SO BRITISH JOURNAL OF CANCER, (**FEB 1999**) Vol. 79, No. 3-4, pp. 423-432.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
ISSN: 0007-0920.
AU Lavie G (Reprint); Kaplinsky C; Toren A; Ainman I; Meruelo D; Mazur Y; Mandel M

AB The mechanism of cell death induction by dimethyl tetrahydroxyhelianthrone (DTHe), a new second-generation photodynamic sensitizer, is analysed in human leukaemic cell lines in comparison with the structurally related hypericin. DTHe has a broad range of light spectrum absorption that enables effective utilization of polychromatic light. Photosensitization of HL-60 cells with low doses of DTHe (0.05 mu M DTHe and 7.1 J cm(-2) light energy) induced rapid apoptosis of greater than or equal to 90% of the cells. At doses greater than or equal to 2 mu M, dying cells assumed morphological necrosis with perinucleolar condensation of chromatin in HL-60 and K-562 cell lines. Although nuclear fragmentation that is characteristic to apoptosis was prevented, DNA digestion to oligonucleosomes proceeded unhindered. Such incomplete apoptosis was more prevalent with the related analogue hypericin throughout most doses of photosensitization. Despite hypericin being a stronger photosensitizer, DTHe exhibited advantageous phototoxic properties to tumour cells, initiating apoptosis at concentrations about threefold lower than hypericin. Photosensitization of the cells induced dissociation of the nuclear envelope, releasing lamins into the cytosol. DTHe also differed from hypericin in effects exerted on the nuclear lamina, causing release of an 86-kDa lamin protein into the cytosol that was unique to DTHe. Within the nucleus, nuclear envelope lamin B underwent covalent **polymerization**, which did not affect apoptotic nuclear fragmentation at low doses of DTHe. At higher doses, **polymerization** may have been extensive enough to prevent nuclear collapse. Hut-78, CD4(+) cells were resistant to the photodynamically activated apoptotic pathway. Beyond the tolerated levels of photodynamic **damage**, these cells died exclusively via necrosis. Hut-78 cells overexpress Bcl-X-L, as well as a truncated Bcl-X-L(tr) isoform that could contribute to the observed resistance to apoptosis.

L5 ANSWER 28 OF 28 SCISEARCH COPYRIGHT 2000 ISI (R)
PY 1996
TI Catalytic cycle of a divanadium complex with salen ligands in O-2 reduction: Two-electron redox process of the binuclear center (salen equals N,N'-ethylenebis(salicylideneamine))
SO JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (**18 DEC 1996**) Vol. 118, No. 50, pp. 12665-12672.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0002-7863.
AU Yamamoto K; Oyaizu K; Tsuchida E (Reprint)
AB In an attempt to provide confirmation for the postulated mechanism of O-2 reduction in vanadium-mediated oxidative **polymerization** of diphenyl disulfide, a series of divanadium complexes containing salen ligand (salen = N,N'ethylenebis(salicylideneamine)) were prepared, characterized, and subjected to reactivity studies toward dioxygen. A divanadium(III, IV) complex, [(salen)VOV(salen)][I-3] (II), was yielded both by treatments of solutions of [(salen)-VOV(salen)][BF4](2) (I) in acetonitrile with excess tetrabutylammonium iodide and by electroreduction of I followed by anion exchange with tetrabutylammonium triiodide. The complex II was characterized by a near-infrared absorption at 7.2 x 10(3) cm(-1) (epsilon = 61.1 M(-1) cm(-1) in acetonitrile) assigned to an intervalence transfer band. A crystallographically determined V(III)-V(IV) distance of 3.568(4) Angstrom is consonant with the classification of II as a weakly coupled Type II mixed-valence vanadium (alpha = 3.1 x 10(-2)). **Oxidation** of the cation [(salen)VOV(salen)](+) with O-2 in dichloromethane yielded spontaneously the deep blue, mixed valent, divanadium(IV, V) species [(salen)VOVO-(salen)](+) which was structurally characterized both as its triiodide (III) and perchlorate (IV) salts. Crystal data for III: triclinic space group P (1) over bar (no. 2), a = 14.973(2) Angstrom, b = 19.481(2) Angstrom, c 14.166(2) Angstrom, alpha = 107.20 (1)degrees, beta = 111.58(1)degrees, gamma = 80.35(1)degrees, V =

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2561.3(9) Angstrom(3), Z = 4, D-calc = 1.953 g/cm(3), mu (MoK alpha) = 31.74 cm(-1), final R = 0.057 and R(w) = 0.065. Crystal data for IV: triclinic space group P (1) over bar (no. 2), a = 11.923(3) Angstrom, b = 14.25(1) Angstrom, c = 11.365(7) Angstrom, alpha = 112.92(5)degrees, beta = 92.76(4)degrees, gamma = 99.13(4)degrees, V = 1743(1) Angstrom(3), Z = 2, D-calc = 1.437 g/cm(3), mu (CuK alpha) = 57.69 cm(-1), final R = 0.042 and R(w) = 0.051. The complexes III and IV were deoxygenated in strongly acidic nonaqueous media to produce [(salen)VOV(salen)](3+) as a high-valent complex whose reversible two-electron redox couple (VOV3+/VOV4+) at 0.44 V vs Ag/AgCl has been confirmed. Its ability to serve as a two-electron **oxidant** provided a unique model of a multielectron redox cycle in oxidative **polymerization**.

=> s (polymerization or polymerisation) and (nitration or peroxidase)
L8 244 (POLYMERIZATION OR POLYMERISATION) AND (NITRATION OR PEROXIDASE)

=> s (oxidation or oxidant or oxidise or oxidize) and (stress or damage)
L7 80154 (OXIDATION OR OXIDANT OR OXIDISE OR OXIDIZE) AND (STRESS OR DAMAGE)

=> s (oxidation or oxidative or oxidant or oxidise or oxidize) and (stress or damage)
L8 136486 (OXIDATION OR OXIDATIVE OR OXIDANT OR OXIDISE OR OXIDIZE) AND (STRESS OR DAMAGE)

=> s l8 and (superoxidase or nitration or peroxidase)
L9 1964 L8 AND (SUPEROXIDASE OR NITRATION OR PEROXIDASE)

=> s l9 and (polymerization)
L10 38 L9 AND (POLYMERIZATION)

=> s l9 and (protein (w) polymerization)
L11 2 L9 AND (PROTEIN (W) POLYMERIZATION)

=> s l6 and l9
L12 38 L6 AND L9

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PROCESSING COMPLETED FOR L11
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L15 ANSWER 1 OF 13 BIOSIS COPYRIGHT 2000 BIOLOGICAL ABSTRACTS INC.
PY 2000
TI A 37-kDa **peroxidase** secreted from liverworts in response to chemical **stress**.
SO Phytochemistry (Oxford), (**October, 2000**) Vol. 55, No. 3, pp. 197-202. print.
ISSN: 0031-9422.
AU Hirata, Toshifumi (1); Ashida, Yoshiyuki; Mori, Hideyuki; Yoshinaga,

09/19/01

Daisuke; Goad, Lionel J.

AB A **peroxidase** was purified from the culture medium of a suspension culture of Marchantia polymorpha (liverwort) after treatment with bornyl acetate, which acts as a chemical **stress** agent to the cells. The **peroxidase** was characterised as a glycoprotein of molecular mass 37-kDa having a pI of about 10 and an optimal pH of 6.5. The **peroxidase** was thermally stable at 50degreeC for up to 60 min. The partial amino acid sequence of the **peroxidase** was determined and found to be dissimilar to the amino acid sequences of other higher plant **peroxidases**. The **oxidative polymerization** of lunularin by this **peroxidase** was examined and the formation of a dimer, a trimer and a tetramer was demonstrated by negative ion Fast Atom Bombardment (FAB)-mass spectroscopy of the reaction products.

L15 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2001 BIOLOGICAL ABSTRACTS INC.
PY 1988
TI IDENTIFICATION OF ACETAMINOPHEN **POLYMERIZATION** PRODUCTS CATALYZED BY HORSERADISH **PEROXIDASE**.
SO J BIOL CHEM, (1988) 263 (31), 16174-16181.
CODEN: JBCHA3. ISSN: 0021-9258.
AU POTTER D W; MILLER D W; HINSON J A
AB Horseradish **peroxidase** catalyzed the H2O2-dependent **oxidation** and **polymerization** of acetaminophen. Six acetaminophen polymers were isolated from horseradish **peroxidase** reaction mixtures by semipreparative high pressure liquid chromatography. Chemical structures were determined by a combination of electron impact and chemical ionization mass spectrometry and 500-MHz proton magnetic resonance spectroscopy. Two dimers, three trimers, and one tetramer were identified. The polymers formed primarily through a covalent bond between carbons ortho to the hydroxyl group, and to a lesser extent, between the carbon ortho to the hydroxyl group and the amino group of another acetaminophen molecule. Greater than 99% of the **polymerization** reaction products were quenched by the addition of 2.1 mM ascorbate. High acetaminophen concentration favored dimer formation, whereas low acetaminophen concentration favored formation of trimers and tetramers. Since approximately 1 mol of H2O2 was consumed per mol of covalent ligand formed between acetaminophen molecules, these products probably result from free radical termination reactions.

L15 ANSWER 3 OF 13 MEDLINE
PY 1998
TI Rickettsia rickettsii infection of the EA.hy 926 endothelial cell line: morphological response to infection and evidence for **oxidative** injury.
SO MICROBIOLOGY, **(1998 Aug)** 144 (Pt 8) 2037-49.
Journal code: 9430538. ISSN: 1465-2080.
AU Eremeeva M E; Silverman D J
AB EA.hy 926 is a permanent human cell line that expresses highly differentiated functions characteristic of human vascular endothelium. Rickettsia rickettsii can efficiently infect and cause a cytopathic effect in EA.hy 926 cells. R. rickettsii produced visible lytic plaques in EA.hy 926 cells at 11 d post-infection (p.i.) following application of a secondary agarose overlay containing 2 micrograms emetine ml-1 and 40 micrograms NaF ml-1 on day 2. Rickettsial growth in EA.hy 926 cells had a similar profile to that occurring in human umbilical vein endothelial cells (HUVEC) and rickettsiae catalysed **polymerization** of actin tails. Intracellular multiplication of R. rickettsii resulted in significant changes in the internal morphology of EA.hy 926 cells, most notably extensive dilatation of the membranes of the endoplasmic reticulum and outer nuclear envelope by 72 h p.i. These events correlated with

significant alterations in the host-cell antioxidant system, including decreased levels of intracellular reduced glutathione and glutathione **peroxidase** activity and increased amounts of intracellular peroxide through to 96 h of infection. These findings are similar to the changes described previously for R. rickettsii-infected HUVEC and suggest that common mechanisms associated with rickettsia-induced **oxidative** injury occur in the two cell lines. EA.hy 926 cells were also used to investigate the influence of the antioxidant alpha-lipoic acid on rickettsial infection. Overnight pretreatment with 1-500 microM alpha-lipoic acid did not prevent cells from being destroyed following infection with rickettsiae. Supplementation of the culture medium with 1 and 10 microM alpha-lipoic acid 2 h after rickettsial inoculation also did not provide any protective effect. However, 100, 200 and 500 microM alpha-lipoic acid increased the viability of infected cells at 96 h to 45, 61 and 72 , respectively compared with 26% for untreated, infected samples. Thiol levels and glutathione **peroxidase** activity in treated, infected cells increased and peroxide content decreased proportionally to increasing alpha-lipoic acid concentrations. Furthermore, treatment with 500 microM alpha-lipoic acid for 72 h p.i. completely prevented ultrastructural changes in infected cells. In conclusion, the permanent endothelial cell line EA.hy 926 is susceptible to injury induced by R. rickettsii infection. Although the cellular changes resulting from infection are not identical in all aspects to that demonstrated previously in HUVEC, the increased reproducibility and convenience of EA.hy 926 cells make them suitable for biochemical and morphological studies.

L15 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2002 ACS
PY 1999
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2002
TI Methods of diagnosis and triage using cell activation measures
SO PCT Int. Appl., 164 pp.
CODEN: PIXXD2
IN Stoughton, Roland B.; Schmid-Schonbein, Geert W.; Hugli, Tony E.; Kistler, Erik
AB Diagnostic methods that rely on the use of one or more assays that assess cellular activation are provided. The assays are performed on whole blood or leukocytes (neutrophils), and indicate individually or in combination the level of cardiovascular cell activation, which is pivotal in many chronic and acute disease states. These results of the assays are used within a clin. framework to support therapeutic decisions such as: further testing for infectious agents, anti-**oxidant** or anti-adhesion therapy, postponement and optimal re-scheduling of high-risk surgeries, classifying susceptibility to and progression rates of chronic disease such as diabetes, organ rejection, atherogenesis, and venous insufficiency; extreme interventions in trauma cases of particularly high risk and activation-lowering therapies. Also provided is compn. derived from a pancreatic homogenate that contains circulating cell activating factors, which can serve as targets for drug screening to identify drug candidates for use in activation lowering therapies. Methods for lowering cell activation by administering protease inhibitors, particularly serine protease inhibitors, are also provided. Kits for performing the methods are also provided.

L15 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2002 ACS
PY **1992**
TI Distribution of iron in different brain regions and subcellular

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compartments in Parkinson's disease
SO Annals of Neurology (**1992**), 32(Suppl.), S101-S104
CODEN: ANNEDB; ISSN: 0364-5134
AU Riederer, P.; Dirr, A.; Goetz, M.; Sofic, E.; Jellinger, K.; Youdim, M. B. H.
AB A review with 28 refs. The essential participation of iron in brain development and maturation indicates that an abnormality of early iron metab. could have profound, even long-term irreversible consequences. Iron deficiency as a cofactor of many heme and nonheme enzymes would alter many metabolic processes, including synthesis of protein, DNA, and RNA. Excess accumulation of tissue iron may lead to **oxidative stress** via formation of oxygen free radicals, which can be highly cytotoxic. Such a phenomenon was implicated in Parkinson's disease (PD). The mechanism of neurotoxicity that leads to degeneration of nigrostriatal dopamine neurons of zona compacta, which in turn leads to a deficiency of dopamine in PD, remains obscure. On numerous occasions, involvement of endogenously or exogenously produced neurotoxins was implicated in the progression of PD. Evidence, however, is lacking, even though synthetic neurotoxins such as N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and 6-hydroxydopamine produce a parkinsonian syndrome in humans and animals. Apparently, during normal aging of human brain there is loss of melanized nigrostriatal neurons. When approx. 40% of the neurons are lost, symptoms (e.g., akinesia, tremor, rigidity) of PD appear. PD is characterized by an accelerated degeneration of pigmented (melanized) dopamine neurons in the pars compact of the substantia nigra (SN). The neurons project to the striatum, where they regulate dopamine-dependent motor activity and synthesize, store, release, and catabolize dopamine as their neurotransmitter. The characteristic pigmentation of the SN is related to formation of neuromelanin as a result of **polymn.** of autoxidative products of dopamine. Dopamine can also be oxidatively metabolized by the enzyme monoamine oxidase (MAO-A and MAO-B), which is highly active in the basal ganglia. The presence of lipid and highly localized large deposits of iron in neurotransmitter-rich brain regions (such as the SN, the globus pallidus, and the caudate nucleus) makes the brain an ideal organ for **oxidative stress** resulting from metal-induced lipid peroxidn. in the presence of H_2O_2. Both **oxidative** deamination and autoxidn. of dopamine result in generation of H_2O_2. In addn., iron activates tyrosine hydroxylase, which could increase dopamine levels. An inability to detoxify H_2O_2 (i.e., catalase, **peroxidase**, glutathione **peroxidase**) could result in its accumulation, and its interaction with Fe^{2+} may promote the Fenton reaction. Iron-induced **oxidative stress** and lipid peroxidn. can proceed optimally with either Fe^{2+} or Fe^{3+}, provided mechanisms exist to facilitate the interconversion of iron between its **oxidn.**-reun. (redox) states. Fe^{3+} can be converted to Fe^{2+} in the presence of endogenous reducing agents, such as ascorbate and glutathione. It is the pigmented melanin-contg. dopamine neurons that degenerate in PD.

L15 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2002 ACS
PY 1993
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TI Acid catalysts and methods of use including as herbicides
SO U.S., 17 pp. Cont.-in-part of U.S. 4,581,925.
CODEN: USXXAM
IN Young, Donald C.
AB Compns. contg. H2SO4 and .gtoreq.1 chalcogen-contg. compd. R1C(:X)R2 (I; R1, R2 = H, NR3R4, OR5, where .gtoreq.1 of R1 and R2 .noteq. H; R3, R4 = H or monovalent org. group; and R5 = divalent org group; the mol ratio of the chalcogen-contg. compd. to H2SO4 is .apprx.1/4 to <2) are catalysts for org. chem. reactions and have herbicidal activity. Acid-catalyzed hydrolysis was demonstrated on 4 replicated test plots of 5 acres each comprising onions at the 1st true-leaf stage (apprx. 1-in. high) infested with malva, cheese weed, night-shade, shepherds purse, pineapple weed and purslane, which were each treated by foliar application of 50 gal/acre of a urea-H2SO4 component have a urea/H2SO4 mol ratio of .apprx.1.1 and contg. urea 14.6, H2SO4 20.8 and H2O 64.6 wt.%. The treatment gave 95-100% kill of all weed species within 48 h after application. There was no **damage** to the onion crop, as evidenced by the lack of foliage browning, spotting, or the like. Further examples using the compns. demonstrated hydrolysis of cellulose to glucose, dissoln. of cowhide, propylene oligomerization, **polymn.** of propylene and butane, polyester prepn. from maleic acid and glycol, benzene alkylation, butane isomerization, demetalation of petroporphyrin-contg. crude oil, and cumene **nitration.**

L15 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2002 ACS
PY **1950**
TI American Society for Testing Materials, Standards, 1950. V. Textiles, soap, fuels, petroleum, aromatic hydrocarbons, antifreezes, water
SO (**1950**), 579 pp.
AB Standards, or tentative standards, adopted or revised in 1950 are given for: definitions of terms relating to textile materials; recommended practice for universal system of yarn numbering; methods of test for bonded fabrics, snag resistance of hosiery, fastness to light of colored textiles, resistance of pile floor coverings to insect **damage**, resistance of textile fabrics to water, and small amts. of Cu and Mn in textiles; specifications and methods of test for asbestos yarns, cloth, and lap; methods of test for magnetic rating of asbestos used for elec. purposes; methods of test and tolerances for glass yarn and continuous filament rayon and estron yarns; mech. roll and sheet felts; methods of test for felt, hard scoured wool in wool in the grease, vegetable matter in scoured wool, fineness of wool and wool tops; chip or granular and solid soaps for low-temp. washing; definitions of terms relating to soap

10/18/01

and other detergents; sieve analysis of coke; tumbler test for coke; gasoline; aviation gasoline; test for acidity of residue from distn. of gasoline and petroleum solvents; analysis of 60 octane no. isooctane-normal heptane ASTM knock test reference fuel blends by infrared spectrophotometry; gaging petroleum and petroleum products; test for existent gum in gasoline; sampling petroleum and petroleum products; test for S in petroleum products; measuring temp. of petroleum and petroleum products; detn. of heat of combustion of liquids by bomb calorimeter; test for water tolerance of aircraft fuels; recommended practice for volume calcns. and corrections in measurement of petroleum and petroleum products; tests for b.-p. range of **polymerization**-grade butadiene, 1,3-butadiene in C4 hydrocarbon mixts. by ultraviolet spectrophotometry, and carbonyl content of butadiene; factors and tables for vol. correction and sp. gr. conversion of liquefied petroleum gases; Diesel fuel oils; heptane no, kauri-butanol value, and nitrocellulose sol. power of hydrocarbon solvents; detn. of purity from f.ps.; tests for S in petroleum products and lubricants by bomb method, and water and sediment by means of centrifuge; tests for Cl in lubricating oils and greases by bomb method, for P in lubricating oils, lubricating additives, and their concentrates, and for sapon. no. of petroleum products by potentiometric titration; testing rust-preventing characteristics of steam-turbine oil in the presence of water; testing elec. insulating oils; tests for apparent viscosity and **oxidation** stability of lubricating greases; **nitration** grade, industrial grade, and industrial 90% benzenes; refined and crude solvent naphthas; **nitration**- and industrial-grade toluenes and xylenes; 5-degree and 10-degree xylenes; distn. of industrial aromatic hydrocarbons; analysis of natural gases by volumetric chem. method; analysis of natural gases and related types of gaseous mixts. by mass spectrometer; test for water vapor content of gaseous fuels by measurement of dewpoint temp.; sampling natural gas; hydrometer-thermometer field tester for engine antifreezes; tests for b.p. of engine antifreezes and for ash content, reserve alky., sp. gr., and water content of concd. engine antifreezes; definitions of terms relating to industrial water; test for Al and Al ion in industrial water; test for total CO_2 and calcn. of carbonate and bicarbonate ions in industrial water; tests for elec. cond., hardness, SiO_2, Na, and K in industrial water; identification of types of microorganisms in industrial water; x-ray diffraction method for identification of cryst. compds. in water-formed deposits; substitute ocean water; reporting results of analysis of industrial water; verification of testing machines and calibration devices for verifying testing machines; recommended practices for designating significant places in specified limiting values; ASTM thermometers. Tentative revisions, submitted in 1959, of standards are given for: testing felt, rayon and estron staple; specifications and methods of test for asbestos roving for elec. purposes.

L15 ANSWER 8 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
PY **2000**
TI Dityrosine cross-linking promotes formation of stable .alpha.-synuclein polymers: Implication of nitrative and **oxidative stress** in the pathogenesis of neurodegenerative synucleinopathies.
SO Journal of Biological Chemistry, (16 Jun 2000) 275.24 (18344-18349). Refs: 48
ISSN: 0021-9258 CODEN: JBCHA3
AU Souza J.M.; Giasson B.I.; Chen Q.; Lee V.M.-Y.; Ischiropoulos H.
AB Intracellular proteinaceous aggregates are hallmarks of many common neurodegenerative disorders, and recent studies have shown that .alpha.-synuclein is a major component of several pathological intracellular inclusions, including Lewy bodies in Parkinson's disease (PD) and glial cell inclusions in multiple system atrophy. However, the molecular mechanisms underlying .alpha.- synuclein aggregation into

filamentous inclusions remain unknown. Since **oxidative** and nitrative **stresses** are potential pathogenic mediators of PD and other neurodegenerative diseases, we asked if **oxidative** and/or nitrative events alter .alpha.-synuclein and induce it to aggregate. Here we show that exposure of human recombinant .alpha.-synuclein to nitrating agents (peroxynitrite ONOO- or myeloperoxidase/H2O2/nitrite) induces formation of nitrated .alpha.-synuclein oligomers that are highly stabilized due to covalent cross-linking via the **oxidation** of tyrosine to form 3,3'-dityrosine. We also demonstrate that **oxidation** and **nitration** of pre-assembled .alpha.-synuclein filaments stabilize these filaments to withstand denaturing conditions and enhance formation of SDS-insoluble, heat-stable high molecular mass aggregates. Thus, these data suggest that **oxidative** and nitrative **stresses** are involved in mechanisms underlying the pathogenesis of Lewy bodies and glial cell inclusions in PD and multiple system atrophy, respectively, as well as .alpha.-synuclein pathologies in other synucleinopathies.

L15 ANSWER 9 OF 15 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
PY **1997**
TI Modified hemoglobin solution, with desired pharmacological properties, does not activate nuclear transcription factor NF-kappa B in human vascular endothelial cells.
SO Artificial Cells, Blood Substitutes, and Immobilization Biotechnology, (1997) 25/1-2 (193-216).
Refs: 70
ISSN: 1073-1199 CODEN: ABSBE4
AU Simoni J.; Simoni G.; Lox C.D.; Prien S.D.; Shires G.T.
AB The aim of the present study was to evaluate the role of hemoglobin (Hb) and the contribution of chemically modified Hb solutions on the activation of nuclear transcription factor, NF-kappa B, and propagation of **oxidative stress** within human vascular endothelial cells. The activation of an **oxidative stress**-sensitive NF-kappa B can be linked with the propagation of an inflammatory state via rapid induction of genes for several pro-inflammatory mediators. Human coronary artery endothelial cells (HCAEC) were cultured on glass coverslips or cell culture plates to confluence. Then, the cells were incubated for up to 16 hours with endothelial basal medium (EBM) supplemented with 1% FBS and test agents in a concentration of 0.1 and 0.2 mmol: 1) unmodified bovine Hb (UHb); 2) modified Hb solution polymerized with glutaraldehyde (GLUT-Hb), and 3) a novel modified Hb solution (Hb-PP-GSH) prepared according to our patented procedure (U.S. Patent No. 5,439,882). The positive control for the NF-kappa B activation study included a treatment of the cells with: 1) endotoxin; IL-1; TNF; and H2O2. Results indicate that Hb's pro-**oxidant** potential was influenced by the type of chemical modification procedure. The GLUT-Hb autoxidation rate, **peroxidase**-like activity and reactivity with H2O2/ferryl species formation were higher as compared to UHb, by 18%, 38% and 30%, respectively. However, pro-**oxidant** potential of Hb-PP-GSH was significantly lower than that of UHb (by 22%, 12% and 28%, respectively). The extent of **oxidative stress** of the HCAEC's was found to be the Hb modification-type and concentration dependent. Although the highest endothelial lipid peroxidation and the largest depletion of intracellular GSH was associated with 0.2 mmol of GLUT-Hb, the Hb-PP-GSH did not produce significant changes when compared to the control cells. The UHb generated a moderate **oxidative stress** to the endothelium. The immunofluorescent and EMSA results indicate a correlation between the type of Hb chemical modification and the induction of NF-kappa B nuclear translocation. We found that GLUT-Hb rapidly activated NF-kappa B and induced nuclear translocation. Treatment of the cells with an increasing amount of UHb leads to the partial nuclear induction of

NF-kappa B. However, Hb-PP-GSH did not activate NF-kappa B directly. In this study, the positive control cells treated with endotoxin, IL-1 or TNF demonstrated full nuclear translocations, whereas H2O2 caused only partial induction. In conclusion, nuclear translocation of NF-kappa B by Hb solutions might be dependent on Hb's pro-**oxidant** potential and extent of Hb-mediated endothelial **oxidative stress**.
Besides the low **oxidative** potential of Hb-PP-GSH, the observed lack of NF-kappa B activation by this Hb solution can be also related to the anti-inflammatory properties of adenosine which is used in our novel modification procedure. In this study, only the Hb-PP-GSH, crosslinked intramolecularly with o-adenosine triphosphate and intermolecularly with o-adenosine, and combined with reduced glutathione, was shown to be non-toxic to the endothelium and promises to be an effective free-Hb based blood substitute.

L15 ANSWER 10 OF 13 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
PY **1997**
TI Antioxidant effects of dietary polymeric grape seed tannins in tissues of rats fed a high cholesterol-vitamin E-deficient diet.
SO Food Chemistry, (1997) 59/1 (135-141).
Refs: 33
ISSN: 0308-8146 CODEN: FOCHDC
AU Tebib K.; Rouanet J.M.; Besancon P.
AB Effects of dietary monomeric and polymeric grape seed tannins on the activity of antioxidant enzymes, total glutathione and level of lipid peroxidation in various tissues were investigated in rats fed a high cholesterol diet poor in vitamin E. They were compared with those in rats receiving a high cholesterol-vitamin E-sufficient diet without addition of tannins. Four groups of rats were studied for 10 weeks: Group 1, sufficient vitamin E diet; Group 2, deficient vitamin E diet; Group 3, deficient vitamin E diet + monomeric tannins (71 mg/kg); Group 4, deficient vitamin E diet + polymeric tannins (71 mg/kg). Compared with a normal vitamin E diet (Group 1), aortic, cardiac, hepatic, intestinal, muscular and renal catalase, glutathione **peroxidase** and superoxide dismutase activities were significantly lower in rats receiving the deficient vitamin E diet (Group 2); polymeric tannins (Group 4), but not monomeric tannins, were able to restore all these enzymic activities. In all tissues and in blood, total glutathione concentration, which was significantly lowered by vitamin E deficiency, was brought to the normal level only with polymeric tannins. Furthermore, the lipid peroxidation in plasma and tissues was significantly reduced in the presence of supplemented polymeric tannins as much as in the presence of vitamin E. It is therefore likely that polymeric grape seed tannins function as antioxidants in vivo, negating the effects of the **oxidative stress** induced by both vitamin E deficiency and atherogenic diet.

L15 ANSWER 11 OF 13 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
PY **1997**
TI Evaluation of hepatic antioxidant systems after intravenous administration of polymeric nanoparticles.
SO Biomaterials, (1997) 18/6 (511-517).
Refs: 40
ISSN: 0142-9612 CODEN: BIMADU
AU Fernandez-Urrusuno R.; Fattal E.; Feger T.; Couvreur P.T.; Therond P.
AB We have investigated the modifications of the levels of intracellular markers of the **oxidative stress** in hepatocytes, after single or repeated injections of poly(isobutyl cyanoacrylate) (PIBCA) and polystyrene (PS) nanoparticles. Nanoparticles were administered intravenously at single doses of 20 and 100 mg kg-1 for 14 days. Levels of reduced (GSH) and oxidized (GSSG) glutathione, superoxide dismutase (SOD), glutathione **peroxidase** (GPx), catalase (CT) and the peroxidation

of membrane lipids were measured. Single and repeated administration of PIBCA and PS nanoparticles induced a transient depletion of GSH and GSSG levels, a transient inhibition of SOD activity and a slight increase in CT activity. However, GPx activity was not modified and lipid peroxidation was not observed, suggesting that hepatocytes are not strongly affected by these modifications. Since nanoparticles do not distribute in hepatocytes, **oxidative** species could proceed from hepatic macrophages, activated after nanoparticle phagocytosis. It is unlikely that poly(alkyl cyanoacrylate) degradation products might be responsible for the **oxidative** attack because non-biodegradable PS nanoparticles induced the same effect. Uptake of polymeric nanoparticles by Kupffer cells in the liver induce modifications in hepatocyte antioxidant systems, probably due to the production of radical oxygen species. However, the depletion in glutathione was not great enough to initiate hepatocyte **damage**, since no changes in lipid peroxidation and reversible alterations were observed. This is an important factor to be considered in the use of polymeric nanoparticles as drug carriers.

L15 ANSWER 12 OF 13 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
PY **1995**
TI Effects of shilajit on biogenic free radicals.
SO Phytotherapy Research, (1995) 9/1 (56-59).
ISSN: 0951-418X CODEN: PHYRES
AU Bhattacharya S.K.; Sen A.P.; Ghosal S.
AB The radicophilicity (antiradical-antioxidant effects) of processed shilajit (SJP) to oxygen-derived free radicals and nitric oxide (NO), and the attendant H2O2 cleaving effect were evaluated. SJP provided complete protection to methyl methacrylate (MMA) against hydroxyl radical-induced **polymerization** and acted as a reversible NO-captobative agent. SJP (25 and 50 mg/kg/day, i.p., for 21 days) induced a dose-related increase in superoxide dismutase (SOD), catalase (CAT) and glutathione **peroxidase** (GPX) activities in frontal cortex and striatum of rats. The data were comparable to those of (-)-deprenyl (2 mg/kg/day, i.p., for 21 days) in respect of SOD and CAT activities. These findings are consistent with the therapeutic uses of shilajit as an Ayurvedic rasayan (rejuvenator) against **oxidative stress** and geriatric complaints.

L15 ANSWER 13 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 1997
TI Reactive oxygen species are involved in nickel inhibition of DNA repair
SO ENVIRONMENTAL AND MOLECULAR MUTAGENESIS, (**1 APR 1997**) Vol. 29, No. 2, pp. 214-218.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0893-6692.
AU Lynn S; Yew F H; Chen K S; Jan K Y (Reprint)
AB Nickel has been shown to inhibit DNA repair in a way that may play a role in its toxicity. Since nickel treatment increases cellular reactive oxygen species (ROS), we have investigated the involvement of ROS in nickel inhibition of DNA repair. Inhibition of glutathione synthesis or catalase activity increased the enhancing effect of nickel on the cytotoxicity of ultraviolet (UV) light. Inhibition of catalase and glutathione **peroxidase** activities also enhanced the retardation effect of nickel on the rejoining of DNA strand breaks accumulated by hydroxyurea plus cytosine-beta-D-arabinofuranoside in UV-irradiated cells. Since DNA **polymerization** and ligation are involved in the DNA-break rejoining, we have investigated the effect of ROS on these two steps in an extract of Chinese hamster ovary cells. Nickel inhibition of the incorporation of (H-3)dTTP into the DNase I-activated calf thymus DNA was stronger than the ligation of poly(dA), oligo(dT), whereas H2O2 was

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more potent in inhibiting DNA ligation than DNA **polymerization**. Nickel, in the presence of H2O2, exhibited a synergistic inhibition on both DNA **polymerization** and ligation and caused protein fragmentation. In addition, glutathione could completely recover the inhibition by nickel or H2O2 alone but only partially recover the inhibition by nickel plus H2O2. Therefore, nickel may bind to DNA-repair enzymes and generate oxygen-free radicals to cause protein degradation in situ. This irreversible **damage** to the proteins involved in DNA repair, replication, recombination, and transcription could be important for the toxic effects of nickel. (C) 1997 Wiley-Liss, Inc.

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(FILE 'HOME' ENTERED AT 17:01:58 ON 19 NOV 2002)

FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 17:02:58 ON 19 NOV 2002

FILE 'BIOSIS, MEDLINE, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 17:11:34 ON 19 NOV 2002

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L11 3 S L9 AND (PROTEIN (W) POLYMERIZATION)
L12 38 S L6 AND L9
L13 31 DUP REM L12 (15 DUPLICATES REMOVED)
L14 3 DUP REM L11 (0 DUPLICATES REMOVED)
L15 19 S L13 AND PY=2000

=> s l8 and (superoxidase or nitration or peroxynitrite)
L16 4677 L8 AND (SUPEROXIDASE OR NITRATION OR PEROXYNITRITE)

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L17 36 L10 AND (POLYMERIZATION OR POLYMERISATION)

=> s l8 and (peroxynitrite)
L18 430 L8 AND (PEROXYNITRITE)

=> s l18 and (polymerization or polymerisation)
L19 1 L18 AND (POLYMERIZATION OR POLYMERISATION)

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L20 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
PY 2002
TI Assessment of **oxidant stress** in vitro and in vivo
SO U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
IN Kim, Hyelock; Roberts-Kirchoff, Elizabeth Starr

09/03/01

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AB There is provided a method of assessing **oxidant stress** by measuring **polymn.** of proteins. Also provided is a marker for **oxidant stress** which includes a polymd. protein. A kit for use in assessing **oxidant stress**, the kit including an assay for detecting polymd. proteins is also provided. A method of lowering **oxidant stress** by administering to a patient an effective amt. of at least one reducing agent is also provided. A pharmaceutical compn. for lowering **oxidant stress**, the pharmaceutical having an effective amt. of reducing agent and a pharmaceutically acceptable carrier is also provided.

L20 ANSWER 3 OF 5 MEDLINE DUPLICATE 1
PY 2002
TI **Peroxynitrite**-induced reactions of synthetic oligo 2'-deoxynucleotides and DNA containing guanine: formation and stability of a 5-guanidino-4-nitroimidazole lesion.
SO BIOCHEMISTRY, (2002 Jun 11) 41 (23) 7508-15.
Journal code: 0370623. ISSN: 0006-2960.
AU Su Bang; Stillwell W G; Wishnok John S; Shallop Anthony J; Jones Roger A; Tannenbaum Steven R
AB **Peroxynitrite** is a strong oxidizing agent that is formed in the reaction of nitric oxide and superoxide anion. It is capable of oxidizing and nitrating a variety of biological targets including DNA, and these modifications may be responsible for a number of pathological conditions and diseases. A recent study showed that **peroxynitrite** reacts with 2',3',5'-tri-O-acetylguanosine to yield a novel compound, tri-O-acetyl-1-beta-D-erythro-pentafuranosyl)-5-guanidino-4-nitroimidazole, and, unlike other **peroxynitrite**-mediated guanine **oxidation** products, it is a stable and significant component formed even at low **peroxynitrite** concentrations. In this work, we studied the in vitro formation of the guanine-derived product, 5-guanidino-4-nitroimidazole, in synthetic oligonucleotides and DNA treated with **peroxynitrite**. When calf thymus DNA or oligonucleotides were reacted with **peroxynitrite** at ambient temperature, the modified base 5-guanidino-4-nitroimidazole was generated along with several other products. The oligonucleotides containing the 5-guanidino-4-nitroimidazole modification were purified by reverse-phase and anion-exchange HPLC and characterized by matrix-assisted laser desorption mass spectrometry. 5-Guanidino-4-nitroimidazole formation in **peroxynitrite**-treated DNA was characterized after enzymatic digestion of the reacted DNA to the nucleoside level. HPLC purification and electrospray ionization mass spectrometry (with selected reaction monitoring) enabled the analysis of this modified nucleoside with high sensitivity. The yield of 5-guanidino-4-nitroimidazole formed in single-stranded DNA was approximately 11-fold higher than that found in duplex DNA. With calf thymus DNA, 5-guanidino-4-nitroimidazole was dose-dependently formed at low **peroxynitrite** concentrations. In stability tests, a synthetic oligonucleotide containing the 5-guanidino-4-nitroimidazole modification was only partially cleaved by hot piperidine and was a weak substrate for Fpg glycosylase repair enzyme; in addition, this site was not cleaved by endonuclease III. These results suggest that nuclear DNA containing 5-guanidino-4-nitroimidazole may not be quickly repaired by DNA repair enzyme systems. Finally, primer extension experiments revealed that this lesion is a potential DNA replication blocker when **polymerization** is catalyzed by polymerase alpha and polymerase I (Klenow fragment, lack of exonuclease activity) but not with human polymerase beta. Replication fidelity experiments further showed that 5-guanidino-4-nitroimidazole may cause G-->T and G-->C transversions in calf thymus polymerase alpha and E. coli polymerase I.

09/661,883

L20 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
PY 2002
TI **Peroxynitrite oxidation** of tubulin sulfhydryls inhibits microtubule **polymerization.**
SO Archives of Biochemistry and Biophysics, (February 15, 2002) Vol. 398, No. 2, pp. 116-124. http://www.academicpress.com/abb. print.
ISSN: 0003-9861.
AU Landino, Lisa M. (1); Hasan, Rifat; McGaw, Ali; Cooley, Sarah; Smith, Abigail W.; Masselam, Kathryn; Kim, Grace
AB Considerable evidence both in vitro and in vivo implicates protein **damage** by **peroxynitrite** as a probable mechanism of cell death. Herein, we report that treatment of bovine brain microtubule protein, composed of tubulin and microtubule-associated proteins, with **peroxynitrite** led to a dose-dependent inhibition of microtubule **polymerization.** The extent of cysteine **oxidation** induced by **peroxynitrite** correlated well with inhibition of microtubule **polymerization.** Disulfide bonds between the subunits of the tubulin heterodimer were detected by Western blot as a result of **peroxynitrite**-induced cysteine **oxidation.** Addition of disulfide reducing agents including dithiothreitol and beta-mercaptoethanol restored a significant portion of the **polymerization** activity that was lost following **peroxynitrite** addition. Thus, **peroxynitrite**-induced disulfide bonds are at least partially responsible for the observed inhibition of **polymerization.** Sodium bicarbonate protected microtubule protein from the **peroxynitrite**-induced inhibition of **polymerization.** Tyrosine nitration of microtubule protein by 1 mM **peroxynitrite** increased approximately twofold when sodium bicarbonate was present whereas the extent of cysteine **oxidation** decreased from 7.5 to 6.3 mol cysteine/mol tubulin. These results indicate that cysteine **oxidation** of tubulin by **peroxynitrite,** rather than tyrosine nitration, is the primary mechanism of inhibition of microtubule **polymerization.**

L20 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
PY 2002
TI Identification of the cysteine residues of tubulin oxidized by **peroxynitrite**
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), TOXI-104 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69CBEZ
AU Landino, Lisa M.; Chen, Alex; Carson, Erin; Doyal, Elizabeth
AB Recently we reported that treatment of bovine brain microtubule protein, composed of tubulin and microtubule-assocd. proteins, with **peroxynitrite** led to a dose-dependent inhibition of microtubule **polymn.** The extent of cysteine **oxidn.,** rather than tyrosine nitration or other types of **peroxynitrite**-induced **damage,** correlated well with the obsd. inhibition of **polymn.** Thus, our current efforts have been directed at identifying the specific cysteines of tubulin and the major microtubule-assocd. proteins, MAP2 and tau, that are oxidized by **peroxynitrite.** We have developed a double-labeling protocol in which thiol-specific fluorescent tags are incorporated into control and **peroxynitrite**-treated protein samples. Because **peroxynitrite**-induced disulfides in tubulin, rather than MAP2 or tau, correlate with inhibition of **polymn.,** we will present the results of our thiol labeling and peptide mapping work performed with purified tubulin.

L20 ANSWER 5 OF 5 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

09921880

PY 2000
TI Dityrosine cross-linking promotes formation of stable .alpha.-synuclein polymers: Implication of nitrative and **oxidative stress** in the pathogenesis of neurodegenerative synucleinopathies.
SO Journal of Biological Chemistry, (16 Jun. 2000) 275(24) (18344-18349). Refs: 46
ISSN: 0021-9258 CODEN: JBCHA3
AU Souza J.M.; Giasson B.I.; Chen Q.; Lee V.M.-Y.; Ischiropoulos H.
AB Intracellular proteinaceous aggregates are hallmarks of many common neurodegenerative disorders, and recent studies have shown that .alpha.-synuclein is a major component of several pathological intracellular inclusions, including Lewy bodies in Parkinson's disease (PD) and glial cell inclusions in multiple system atrophy. However, the molecular mechanisms underlying .alpha.-synuclein aggregation into filamentous inclusions remain unknown. Since **oxidative** and nitrative **stresses** are potential pathogenic mediators of PD and other neurodegenerative diseases, we asked if **oxidative** and/or nitrative events alter .alpha.-synuclein and induce it to aggregate. Here we show that exposure of human recombinant .alpha.-synuclein to nitrating agents (**peroxynitrite**/CO2 or myeloperoxidase/H2O2/nitrite) induces formation of nitrated .alpha.-synuclein oligomers that are highly stabilized due to covalent cross-linking via the **oxidation** of tyrosine to form o,o'-dityrosine. We also demonstrate that **oxidation** and nitration of pre-assembled .alpha.-synuclein filaments stabilize these filaments to withstand denaturing conditions and enhance formation of SDS-insoluble, heat-stable high molecular mass aggregates. Thus, these data suggest that **oxidative** and nitrative **stresses** are involved in mechanisms underlying the pathogenesis of Lewy bodies and glial cell inclusions in PD and multiple system atrophy, respectively, as well as .alpha.-synuclein pathologies in other synucleinopathies.

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L21 3614 (CYTOCHROME (W) C) AND (PEROXYNITRITE OR SUPEROXIDE)

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L22 3 L21 AND (POLYMERIZATION OR POLMYMERISATION)

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L23 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
PY 2002
TI Assessment of oxidant stress in vitro and in vivo
SO U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
IN Kim, Hyesook; Roberts-Kirchoff, Elizabeth Starr
AB There is provided a method of assessing oxidant stress by measuring **polymn.** of proteins. Also provided is a marker for oxidant stress which includes a polymd. protein. A kit for use in assessing oxidant stress, the kit including an assay for detecting polymd. proteins is also provided. A method of lowering oxidant stress by administering to a patient an effective amt. of at least one reducing agent is also provided. A pharmaceutical compn. for lowering oxidant stress, the pharmaceutical having an effective amt. of reducing agent and a pharmaceutically

acceptable carrier is also provided.

L23 ANSWER 2 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2002
TI Integrins engage mitochondrial function for signal transduction by a mechanism dependent on Rho GTPases
SO JOURNAL OF CELL BIOLOGY, (22 JUL 2002) Vol. 158, No. 2, pp. 357-369. Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021 USA.
ISSN: 0021-9525.
AU Werner E (Reprint); Werb Z
AB We show here the transient activation of the small GTPase Rac, followed by a rise in reactive oxygen species (ROS), as necessary early steps in a signal transduction cascade that lead to NFkappaB activation and collagenase-1 (CL-1)/matrix metalloproteinase-1 production after integrin-mediated cell shape changes. We show evidence indicating that this constitutes a new mechanism for ROS production mediated by small GTPases. Activated RhoA also induced ROS production and up-regulated CL-1 expression. A Rac mutant (L37) that prevents reorganization of the actin cytoskeleton prevented integrin-induced CL-1 expression, whereas mutations that abrogate Rac binding to the neutrophil NADPH membrane oxidase in vitro (H26 and N33) did not. Instead, ROS were produced by integrin-induced changes in mitochondrial function, which were inhibited by Bcl-2 and involved transient membrane potential loss. The cells showing this transient decrease in mitochondrial membrane potential were already committed to CL-1 expression. These results unveil a new molecular mechanism of signal transduction triggered by integrin engagement where a global mitochondrial metabolic response leads to gene expression rather than apoptosis.

L23 ANSWER 3 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
PY 2001
TI Hypertonic saline alteration of the PMN cytoskeleton: Implications for signal transduction and the cytotoxic response.
SO Journal of Trauma Injury Infection and Critical Care, (February, 2001) Vol. 50, No. 2, pp. 216-217. print.
ISSN: 1079-6061.
AU Chesla, David J.; Moore, Ernest E. (1); Musters, Rene J.; Biffl, Walter L.; Silliman, Christopher C.
AB Background: Recognition that hypertonic saline (HTS) modulates the inflammatory response has renewed interest in this agent for postinjury resuscitation. Changes in extracellular tonicity alter cell shape and are accompanied by cytoskeletal reorganization. Recent evidence suggests that cytoskeletal reorganization is critical for receptor-mediated signal transduction. We hypothesized that HTS-induced changes in the cytoskeleton interfere with cytotoxic signal transduction. Methods: Isolated neutrophils (PMNs) were incubated in HTS (Na+ = 181 mmol/L) and activated with N-formylmethionyl-leucyl-phenylalanine (receptor-mediated) or phorbol myristate (receptor independent). Actin **polymerization** was assessed by digital image microscopy and flow cytometry. PMN **superoxide** anion (O_2^-) production and p38 MAPK activation was measured by reduction of **cytochrome c** and Western blot. Pretreatment with cytochalasin B was used to disrupt HTS-induced actin reorganization. Results: HTS inhibited receptor-mediated cytoskeletal reorganization and attenuated p38 MAPK activation and O_2^- production. HTS had no effect on receptor-independent O_2^- production. Cytoskeletal disruption (cytochalasin B) prevented HTS attenuation of receptor-mediated p38 MAPK activation. Conclusion: HTS attenuates the PMN cytotoxic response by interfering with intracellular signal transduction. Changes in the actin cytoskeleton appear to modulate receptor-mediated p38

09/1880

MAPK signaling.

L23 ANSWER 4 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2000
TI **Superoxide** dismutase as a target for the selective killing of cancer cells
SO NATURE, 21 SEP 2000 Vol. 407, No. 6802, pp. 390-395.
Publisher: MACMILLAN PUBLISHERS LTD, PORTERS SOUTH, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
ISSN: 0028-0836.
AU Huang P (Reprint); Feng L; Oldham E A; Keating M J; Plunkett W
AB **Superoxide** dismutases (SOD) are essential enzymes that eliminate **superoxide** radical (O-2(-)) and thus protect cells from damage induced by free radicals 1-3. The active O-2(-) production and low SOD activity in cancer cells 3-7 may render the malignant cells highly dependent on SOD for survival and sensitive to inhibition of SOD. Here we report that certain oestrogen derivatives selectively kill human leukaemia cells but not normal lymphocytes. Using complementary DNA microarray and biochemical approaches, we identify SOD as a target of this drug action and show that chemical modifications at the 2-carbon (2-OH, 2-OCH3) of the derivatives are essential for SOD inhibition and for apoptosis induction. Inhibition of SOD causes accumulation of cellular O-2(-) and leads to free-radical-mediated damage to mitochondrial membranes, the release of **cytochrome c** from mitochondria and apoptosis of the cancer cells. Our results indicate that targeting SOD may be a promising approach to the selective killing of cancer cells, and that mechanism-based combinations of SOD inhibitors with free-radical-promoting agents may have clinical applications.

L23 ANSWER 5 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)
PY 2000
TI Arabidopsis ATP A2 peroxidase. Expression and high-resolution structure of a plant peroxidase with implications for lignification
SO PLANT MOLECULAR BIOLOGY, (SEP 2000) Vol. 44, No. 2, pp. 231-243.
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.
ISSN: 0167-4412.
AU Ostergaard L; Teilum K; Mirza O; Mattsson O; Petersen M; Welinder K G; Mundy J; Gajhede M; Henriksen A (Reprint)
AB Lignins are phenolic biopolymers synthesized by terrestrial, vascular plants for mechanical support and in response to pathogen attack. Peroxidases have been proposed to catalyse the dehydrogenative **polymerization** of monolignols into lignins, although no specific isoenzyme has been shown to be involved in lignin biosynthesis. Recently we isolated an extracellular anionic peroxidase, ATP A2, from rapidly lignifying Arabidopsis cell suspension culture and cloned its cDNA. Here we show that the Atp A2 promoter directs GUS reporter gene expression in lignified tissues of transgenic plants. Moreover, an Arabidopsis mutant with increased lignin levels compared to wild type shows increased levels of ATP A2 mRNA and of a mRNA encoding an enzyme upstream in the lignin biosynthetic pathway. The substrate specificity of ATP A2 was analysed by X-ray crystallography and docking of lignin precursors. The structure of ATP A2 was solved to 1.44 Angstrom resolution at 100 K. Docking of p-coumaryl, coniferyl and sinapyl alcohol in the substrate binding site of ATP A2 were analysed on the basis of the crystal structure of a horseradish peroxidase C-CN-ferulic acid complex. The analysis indicates that the precursors p-coumaryl and coniferyl alcohols are preferred by ATP A2, while the oxidation of sinapyl alcohol will be sterically hindered in ATP A2 as well as in all other plant peroxidases due to an overlap with the conserved Pro-139. We suggest ATP A2 is involved in a complex regulation of the covalent cross-linking in the plant cell wall.

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L23 ANSWER 6 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
PY 1997
TI Ca-2+-independent permeabilization of the inner mitochondrial membrane by **peroxynitrite** is mediated by membrane protein thiol cross-linking and lipid peroxidation.
SO Archives of Biochemistry and Biophysics, (1997) Vol. 345, No. 2, pp. 243-250.
ISSN: 0003-9861.
AU Radi, R. (1); Thomson, L.; Fagian, M. M.; Costa, A. D. T.; Radi, R.; Vercesi, A. E.
AB **Peroxynitrite** anion, the reaction product of **superoxide** and nitric oxide, is a potent biological oxidant, which inactivates mammalian heart mitochondrial NADH-coenzyme Q reductase (complex I), succinate dehydrogenase (complex II), and ATPase, without affecting **cytochrome c** oxidase (complex IV). In this paper, we evaluated the effect of **peroxynitrite** on mitochondrial membrane integrity and permeability under low calcium concentration. Phosphate buffer was used in most of our experiments since Hepes, Tris, mannitol, and sucrose were found to inhibit the oxidative chemistry of **peroxynitrite**. **Peroxynitrite** (0.1-1.0 mM) caused a dose-dependent decrease in the ability of mitochondria to build up a membrane potential when N,N,N',N'-tetramethyl-p-phenylenediamine/ascorbate were used as substrate. Elimination of the membrane potential was accompanied by penetration of the osmotic support (KCl/NaCl) into the matrix as judged by the parallel occurrence of mitochondrial swelling. This swelling was partially inhibited by dithiothreitol (DTT) or butylated hydroxytoluene (BHT) and was insensitive to ethylene glycol-bis(beta-aminoethyl ether)N,N,N',N'-tetraacetic acid, ADP, and cyclosporin A. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of solubilized membrane proteins indicated that alterations in membrane permeability were associated with the production of protein aggregates due to membrane protein thiol cross-linking. The protective effect of DTT on both mitochondrial swelling and protein **polymerization** suggests the involvement of disulfide bonds in the membrane permeabilization process. In addition, the increase in thiobarbituric acid-reactive substances and the partial inhibitory effect of BHT indicate the occurrence of lipid peroxidation. These results support the idea that under our experimental conditions **peroxynitrite** causes mitochondrial structural and functional alterations by Ca-2+-independent mechanisms through lipid peroxidation and protein sulfhydryl oxidation.

L23 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2002 ACS
PY 1997
TI Hydrogels containing water-soluble fullerene
SO Gaofenzi Xuebao (1997), (1), 122-125
CODEN: GAXUE8; ISSN: 1001-3304
AU Chen, Liwei; Cheng, Lei; Hong, Han; Li, Zichen; Zhou, Kuiliang; Li, Fumian
AB C60 can react easily with 2-ethanolamine forms a water-sol. deriv. C60-AE. C60-AE can be further modified by acryloyl chloride and methacryloyl chloride to give fullerene-contg. monomers (C60-AE-AC and C60-AE-MAC). A water-sol. fullerene macromer (C60-JD400) was also obtained by reaction of C60 with amino group-terminated polypropylene glycol (Jeffamine D400). Three kinds of C60-contg. hydrogels are prepd. by adsorption of C60-JD400 by poly(N-isopropylacrylamide) hydrogel, by **polymn.** of N-isopropylacrylamide (I) in C60-JD400 aq. soln. to give a semi-IPN hydrogel, and by copolymn. I with C60-AE-AC or C60-AE-MAC. The **superoxide** anion (O2-) level under visible light irradn. in systems contg. C60-JD400 was investigated by traditional **cytochrome C** method. **Cytochrome C**

09/33401

is reduced by **superoxide** anion and the absorbance of reduced **cytochrome C** increased with increasing of irradn. time.

L23 ANSWER 9 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
PY 1997
TI Chemotactic 5-oxo-eicosatetraenoic acids induce oxygen radical production, Ca-2+-mobilization, and actin reorganization in human eosinophils via a pertussis toxin-sensitive G-protein.
SO Journal of Investigative Dermatology, (1997) Vol. 108, No. 1, pp. 103-112. ISSN: 0022-202X.
AU Czech, Wolfgang (1); Barbisch, Michael; Tenscher, Kirsten; Schoepf, Erwin; Schroeder, Jens-Michael; Norgauer, Johannes
AB The arachidonic acid metabolites 5-oxo-(6E,8Z,11Z,14Z)-eicosatetraenoic acid (5oxoETE) and 5-oxo-15-hydroxy-(6E,8Z,11Z,13E)-eicosatetraenoic acid (5oxoHETE) are potent eosinophil chemotaxins. Here, the activation profile of 5-oxo-eicosanoids in eosinophils was further characterized and compared to other eosinophil activators such as complement fragment C5a (C5a), platelet-activating factor (PAF), interleukin-5 (IL-5), and phorbol ester (PMA). Flow cytometric studies revealed a rapid and transient actin **polymerization** upon stimulation by both 5-oxo-eicosanoids. Desensitization studies using actin **polymerization** as the parameter indicated cross-desensitization between the two 5-oxo-eicosanoids but revealed no interference with the response to other chemotaxins. Fluorescence measurements with Fura-2-labeled eosinophils in the presence of EGTA indicated Ca-2+-mobilization from intracellular stores by 5oxoETE and 5oxoHETE. Both 5-oxo-eicosanoids stimulated the production of reactive oxygen metabolites as demonstrated by luminol-dependent chemiluminescence, **superoxide** dismutase-inhibitable **cytochrome C** reduction, and flow cytometric dihydrorhodamine-123 analysis. At optimal concentrations the changes induced by 5-oxo-eicosanoids were comparable to those obtained by C5a and PAF, whereas IL-5 and PMA induced only a restricted pattern of cell responses. Cell responses elicited by 5-oxo-eicosanoids were inhibited by pertussis toxin, indicating coupling of the putative 5-oxo-eicosanoid-receptor to G-proteins. These results indicate that 5-oxo-eicosanoids are strong activators of eosinophils with comparable biologic activity to the eosinophil chemotaxins C5a and PAF. These findings point to a role of 5-oxo-eicosanoids in the pathogenesis of eosinophilic inflammation as chemotaxins as well as activators of pro-inflammatory activities.

L23 ANSWER 9 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
PY 1997
TI The monocyte chemotactic protein-4 induces oxygen radical production, actin reorganization, and CD11b up-regulation via a pertussis toxin-sensitive G-protein in human eosinophils.
SO Biochemical and Biophysical Research Communications, (Nov. 7, 1997) Vol. 241, No. 1, pp. 92-98. ISSN: 0006-291X.
AU Tenscher, Kirsten (1); Metzner, Beatrix; Hofmann, Clemens; Schoepf, Erwin; Norgauer, Johannes
AB The novel human CC-chemokine monocyte chemotactic protein-4 (MCP-4) is a chemotaxin for eosinophils. Here, the biological activities and the activation profile of MCP-4 was further characterized in eosinophils and compared to other activators such as platelet activating factor (PAF), Eotaxin and RANTES. As demonstrated by luminol-dependent chemiluminescence and **superoxide** dismutase-inhibitable **cytochrome C** reduction MCP-4 stimulated the production of reactive oxygen metabolites. Furthermore, MCP-4 induced up-regulation

of the integrin CD11b. Flow cytometric studies revealed rapid and transient actin **polymerization** upon stimulation with MCP-4. At optimal concentrations the changes induced by MCP-4 were weaker than the effects after stimulation with PAF and comparable to those obtained by RANTES and Eotaxin. Cell responses elicited by MCP-4 were inhibited by pertussis toxin indicating involvement of Gi-proteins in this signal pathway. These findings point to a role of MCP-4 in the pathogenesis of eosinophilic inflammation as chemotaxin as well as activator of pro-inflammatory effector functions.

L23 ANSWER 11 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5

PY 1996

TI Recombinant human eotaxin induces oxygen radical production, Ca-2+-mobilization, actin reorganization, and CD11b upregulation in human eosinophils via a pertussis toxin-sensitive heterotrimeric guanine nucleotide-binding protein.

SO Blood, (1996) Vol. 88, No. 6, pp. 3145-3150.
ISSN: 0006-4971.

AU Jenscher, Kirsten (1); Metzner, Beatrix; Schnepf, Erwin; Norgauer, Johannes; Czech, Wolfgang

AB The novel human CC-chemokine Eotaxin is a potent and selective chemotaxin for eosinophils. Here, the biological activities and the activation profile of Eotaxin were further characterized and compared with those of other eosinophil chemotaxins such as complement fragment C5a (C5a), platelet-activating factor (PAF), and RANTES in human eosinophils. Eotaxin stimulated the production of reactive oxygen metabolites as shown by luminol-dependent chemiluminescence and **superoxide** dismutase-inhibitable **cytochrome C** reduction. Furthermore, Eotaxin induced upregulation of the integrin CD11b. In addition, fluorescence measurements with Fura-2-labeled eosinophils in the presence of EGTA indicated Ca-2+-mobilization from intracellular stores by Eotaxin. Flow cytometric studies showed rapid and transient actin **polymerization** on stimulation with Eotaxin. At optimal concentrations, the changes induced by Eotaxin were comparable with those obtained by C5a, PAF, and RANTES. Cell responses elicited by Eotaxin were inhibited by pertussis toxin, indicating coupling of its putative receptor to heterotrimeric guanine nucleotide-binding proteins. These results indicate that Eotaxin is a strong activator of eosinophils with biological activity comparable with those of the eosinophil chemotaxins C5a, PAF, and RANTES. These findings point to a role of Eotaxin in the pathogenesis of eosinophilic inflammation as a chemotaxin as well as an activator of proinflammatory effector functions.

L23 ANSWER 12 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6

PY 1993

TI Spin trapping of **superoxide** radicals following stimulation of neutrophils with fMLP is temperature dependent.

SO Free Radical Biology & Medicine, (1993) Vol. 15, No. 4, pp. 425-433.
ISSN: 0891-5849.

AU Taniguwa, Toru; Kotake, Yashige (1); Reinko, Lester A.

AB Oxygen radical formation by human neutrophils stimulated with a chemotactic peptide, formyl-methionyl-leucyl-phenylalanine (fMLP), was studied through the use of spin trapping and **superoxide** dismutase-inhibitable reduction of oxidized **cytochrome c** . Both methods provided comparable data on temperature-dependent kinetics of **superoxide** radical formation, but hydroxyl radicals were also detected in spin-trapping experiments. When **superoxide** generation was monitored at 37 degree C, the respiratory burst lasted only a few minutes. If the neutrophils were stimulated at 37 degree C, but

superoxide measurements were done at room temperature, the respiratory burst was again transient. However, neutrophils persistently generated **superoxide** when both stimulation and subsequent measurements were performed at room temperature. In the presence of the actin **polymerization** inhibitor, cytochalasin B, **superoxide** generation was persistent, even when measurements were conducted at 37 degree C. A possible explanation for these observations is that the fMLP receptor complexes quickly aggregate and are internalized at physiological temperature, but not at room temperature. Very little **superoxide** was formed if cells were kept at a temperature of 4 degree C for 1 h prior to fMLP addition, which is consistent with decreased expression of the fMLP receptor at cold temperatures.

L23 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2002 ACS
PY 1990
1990
1990
1990
TI Redox **polymerization** diagnostic test composition and method for immunoassay and nucleic acid hybridization assay
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
IN Oster, Gerald; Davis, Barnum J.
AB A diagnostic test compn. for detecting and measuring an analyte possessing biol. activity comprises (a) a redox catalyst system capable of converting a monomer to a polymer, the monomer capable of undergoing addn. **polymn.**, the redox catalyst system comprising .gtoreq.1 chem. moieties with 1) the analyte comprising .gtoreq.1 such moiety or 2) in the case that the analyte lacks a redox catalyst property, the analyte is linked by a specific ligand to .gtoreq.1 such moiety or is linked by the specific ligand to a generator of .gtoreq.1 such moiety; and; (b) .gtoreq.1 monomer capable of undergoing addn. **polymn.** Immunoassays and nucleic acid hybridization assays using redox **polymn.** are described. Thus, glucose oxidase coupled to antibody is reacted with an immobilized antigen spot on a glass slide, unbound conjugate is washed off, and the slide is dipped into a soln. contg. Ca acrylate 1%, glucose 5%, and ascorbate acid 0.5% for 10 min to form a grossly visible white ppt. at the site of the antigen.

L23 ANSWER 13 OF 13 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
PY 1990
TI STIMULUS SPECIFIC DEACTIVATION OF CHEMOTACTIC FACTOR INDUCED CYCLIC AMP RESPONSE AND SUPER OXIDE GENERATION BY HUMAN NEUTROPHILS.
SO J CLIN INVEST, (1990) 86 (3), 736-747.
CODEN: JCINAO. ISSN: 0021-9738.
AU SIMCHOWITZ L; ATKINSON J P; SPILBERG I
AB The responses of isolated human peripheral neutrophils to either simultaneous or sequential additions of 2 chemotactic factors were studied. Simultaneous additions of formyl-methionyl-leucyl-phenylalanine (1-100 nM) and the 5th component of complement, C5a (1-10 mu.l/ml), evoked partially additive responses of membrane depolarization as measured by the fluorescent dye 3,3'-dipropyl-thiocarbocyanine, a transient elevation of intracellular cAMP, and **superoxide** (O_2^-) generation as assessed by ferricytochrome c reduction. Preincubation of the cells with either formyl-methionyl-leucyl-phenylalanine or C5a alone caused dose-dependent inhibition of the depolarization, the cAMP increase, and O_2^- release induced by a subsequent exposure to an optimal dose of the same stimulus, i.e., deactivation occurred. In contrast, when cells were treated with 1 chemotactic factor and then exposed to the other stimulus, the cells exhibited a normal response of peak depolarization, the rise in

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cAMP, and O2- production i.e., cross-deactivation failed to occur. Deactivation of these phenomena is apparently stimulus specific. Further, these observations are consistent with the hypothesis that cross-deactivation of chemotaxis is mediated by 1 or more processes that are irrelevant to O2- generation, and that occur distal to the depolarization and cAMP steps in the sequence of neutrophil activation: possibly microtubule **polymerization** and orientation.

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=> LOG Y

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NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FORESE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 27, 2002;

08/03/01

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NEWS 19 Aug 14 Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
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NEWS 21 Aug 14 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
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NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
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L1 7166 (PROTEIN (W) AGGREGATION)

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S-++++++++++++++ IS NOT A RECOGNIZED COMMAND
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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l1 and (peroxynitrite or cytochrome)
L2 108 L1 AND (PEROXYNITRITE OR CYTOCHROME)

=> dup rem l1
PROCESSING IS APPROXIMATELY 16% COMPLETE FOR L1
PROCESSING IS APPROXIMATELY 44% COMPLETE FOR L1
PROCESSING IS APPROXIMATELY 86% COMPLETE FOR L1
PROCESSING COMPLETED FOR L1
L3 4576 DUP REM L1 (2791 DUPLICATES REMOVED)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L4 45 DUP REM L2 (73 DUPLICATES REMOVED)

=> s l4 and (peroxynitrite)
L5 13 L4 AND (PEROXYNITRITE)

=> s l4 and (cytochrome (w) c)
L6 33 L4 AND (CYTOCHROME (W) C)

=> d 1-13 l4 so ti au py ab

L4 ANSWER 1 OF 45 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO Journal of Biological Chemistry, (29 Mar 2002) 277/13 (10949-10954).
Refs: 27
ISSN: 0021-9258 CODEN: JBCHA3
TI Heterogeneous Rieske proteins in the **cytochrome** b(6)f complex of Synechocystis PCC6803.
AU Schneider D.; Berry-Lowe S.; Boehm R.; Schmidt C.L.; Seidler A.; Soppa B.
PY 2002
AB The completely sequenced genome of the cyanobacterium Synechocystis PCC6803 contains three open reading frames, petC1, petC2, and petC3, encoding putative Rieske iron-sulfur proteins. After heterologous overexpression, all three gene products have been characterized and shown to be Rieske proteins as typified by sequence analysis and EPR spectroscopy. Two of the overproduced proteins contained already incorporated iron-sulfur clusters, whereas the third one formed unstable aggregates, in which the Fe/S cluster had to be reconstituted after refolding of the denatured protein. Although EPR spectroscopy showed typical Fe/S signals for all Rieske proteins, an unusual low midpoint potential was revealed for PetC3 by EPR redox titration. Detailed characterization of Synechocystis membranes indicated that all three Rieske proteins are expressed under physiological conditions. Both for PetC1 and PetC3 the association with the thylakoid membrane was shown, and

both could be identified, although in different amounts, in the isolated **cytochrome** b(6)f complex. The considerably lower redox potential determined for PetC9 indicates heterogeneous **cytochrome** b(6)f complexes in Synechocystis and suggests still to be established alternative electron transport routes.

L4 ANSWER 2 OF 95 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

SO Biochemistry, (April 16, 2002) Vol. 41, No. 15, pp. 4872-4882. http://pubs.acs.org/journals/bichaw/. print. ISSN: 0006-2960.

TI Molecular architecture of the thylakoid membrane: Lipid diffusion space for plastoquinone.

AU Kirchhoff, H. (1); Mukherjee, U.; Galla, H.-J.

PY 2002

AB We have determined the stoichiometric composition of membrane components (lipids and proteins) in spinach thylakoids and have derived the molecular area occupied by these components. From this analysis, the lipid phase diffusion space, the fraction of lipids located in the first protein solvation shell (boundary lipids), and the plastoquinone (PQ) concentration are derived. On the basis of these stoichiometric data, we have analyzed the motion of PQ between photosystem (PS) II and **cytochrome** (cyt.) bf complexes in this highly protein obstructed membrane (protein area about 70%) using percolation theory. This analysis reveals an inefficient diffusion process. We propose that distinct structural features of the thylakoid membrane (grana formation, microdomains) could help to minimize these inefficiencies and ensure a non-rate limiting PQ diffusion process. A large amount of published evidence supports the idea that higher protein associations exist, especially in grana thylakoids. From the quantification of the boundary lipid fraction (about 60%), we conclude that protein complexes involved in these associations should be spaced by lipids. Lipid-spaced **protein aggregations** in thylakoids are qualitatively different to previously characterized associations (multisubunit complexes, supercomplexes). We derive a hierarchy of protein and lipid interactions in the thylakoid membrane.

L4 ANSWER 3 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

SO Human Molecular Genetics, (1 May 2002) 11/9 (1137-1151). Refs: 47 ISSN: 0964-6906 CODEN: HMGEE5

TI Heat shock protein 27 prevents cellular polyglutamine toxicity and suppresses the increase of reactive oxygen species caused by huntingtin.

AU Wyttenbach A.; Sauvageot O.; Carmichael J.; Diaz-Latoud C.; Arrigo A.-P.; Rubinsztein D.C.

PY 2002

AB Neuronal loss and intraneuronal protein aggregates are characteristics of Huntington's disease (HD), which is one of 10 known neurodegenerative disorders caused by an expanded polyglutamine [poly(Q)] tract in the disease protein. N-terminal fragments of mutant huntingtin produce intracellular aggregates and cause toxicity. Several studies have shown that chaperones suppress poly-Q) aggregation and toxicity/cell death, but the mechanisms by which they prevent poly(Q)-mediated cell death remain unclear. In the present study, we identified heat shock protein 27 (HSP27) as a suppressor of poly(Q) mediated cell death, using a cellular model of HD. In contrast to HSP40/70 chaperones, we showed that HSP27 suppressed poly(Q) death without suppressing poly-Q) aggregation. We tested the hypotheses that HSP27 may reduce poly(Q)-mediated cell death either by binding **cytochrome** c and inhibiting the mitochondrial death pathway or by protecting against reactive oxygen species (ROS). While poly(Q)-induced cell death was reduced by inhibiting **cytochrome**

c (cyt c) release from mitochondria, protection by HSP27 was regulated by its phosphorylation status and was independent of its ability to bind to cyt c. However, we observed that mutant huntingtin caused increased levels of ROS in neuronal and non-neuronal cells. ROS contributed to cell death because both N-acetyl-L-cysteine and glutathione in its reduced form suppressed poly(Q)-mediated cell death. HSP27 decreased ROS in cells expressing mutant huntingtin, suggesting that this chaperone protects cell against oxidative stress. We propose that a poly(Q) mutation can induce ROS that directly contribute to cell death and that HSP27 is an antagonist in this process.

L4 ANSWER 4 OF 95 CAPLUS COPYRIGHT 2002 ACS
SO Biochemical and Biophysical Research Communications (2002), 294(5), 1130-1137
CODEN: BBRCA9; ISSN: 0006-291X
TI Dysfunction of rat liver mitochondria by selenite: Induction of mitochondrial permeability transition through thiol-oxidation
AU Kim, Tae-soo; Jeong, Dae-won; Yun, Byung Yup; Kim, Ick Young
PY 2002
AB Selenium is an essential trace element in mammals and is thought to play a chemopreventive role in human cancer, possibly by inducing tumor cell apoptosis. Mitochondria play a pivotal role in the induction of apoptosis in many cell types. The effects of selenite on mitochondrial function were therefore investigated. Selenite induced the oxidn. and crosslinking of protein thiol groups, mitochondrial permeability transition (MPT), a decrease in the mitochondrial membrane potential, and the release of **cytochrome** c in mitochondria isolated from rat liver. Induction of the MPT by selenite was prevented by cyclosporin A, EGTA, or N-ethylmaleimide. These results thus indicate that selenite induces the MPT as a result of direct modification of protein thiol groups, resulting in the release of **cytochrome** c and a loss of mitochondrial membrane potential.

L4 ANSWER 5 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO Biochemical Pharmacology, (1 Sep 2002) 64(5-6) (1037-1048).
Refs: 146
ISSN: 0006-2952 CODEN: BCPCA6
TI Glutathione, iron and Parkinson's disease.
AU Bharath S.; Hsu M.; Kaur D.; Rajagopalan S.; Andersen J.K.
PY 2002
AB Parkinson's disease (PD) is a progressive neurodegenerative disease involving neurodegeneration of dopaminergic neurons of the substantia nigra (SN), a part of the midbrain. Oxidative stress has been implicated to play a major role in the neuronal cell death associated with PD. Importantly, there is a drastic depletion in cytoplasmic levels of the thiol tripeptide glutathione within the SN of PD patients. Glutathione (GSH) exhibits several functions in the brain chiefly acting as an antioxidant and a redox regulator. GSH depletion has been shown to affect mitochondrial function probably via selective inhibition of mitochondrial complex I activity. An important biochemical feature of neurodegeneration during PD is the presence of abnormal protein aggregates present as intracytoplasmic inclusions called Lewy bodies. Oxidative damage via GSH depletion might also accelerate the build-up of defective proteins leading to cell death of SN dopaminergic neurons by impairing the ubiquitin-proteasome pathway of protein degradation. Replenishment of normal glutathione levels within the brain may hold an important key to therapeutics for PD. Several reports have suggested that iron accumulation in the SN patients might also contribute to oxidative stress during PD. COPYRGT. 2002 Elsevier Science Inc. All rights reserved.

L4 ANSWER 6 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

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SO Life Sciences, (28 Jun 2002) 71/6 (693-705).
Refs: 45
ISSN: 0024-3205 CODEN: LIFSAK
TI Three different pathways for human LDL oxidation are inhibited in vitro by water extracts of the medicinal herb Achyrocline satureoides.
AU Gugliucci A.; Menini T.
PY 2002
AB In this study we investigated the antioxidant properties of one herbal preparation widely used in complementary and alternative medicine in large areas of the world: Achyrocline satureoides (AS), popularly known as "marcela". Although rich in flavonoids, the ethnopharmacological uses of this plant do not include atherosclerosis prevention. Furthermore, no study had been conducted so far exploring the antioxidant activity of Achyrocline satureoides vis-a-vis human LDL oxidation, which is the compelling issue in pinpointing potential cardioprotective new uses for a traditional remedy. We explored the effects of AS extracts on human LDL oxidation, employing 3 different systems which are thought to play a role in oxidation of LDL in the arterial wall: copper, **peroxynitrite**, and lipoxygenase. Oxidation was monitored by conjugate dienes, TBARS formation and aggregation of apoB using SDS-PAGE. In copper-initiated oxidation a dose dependent inhibition of the initiation and propagation of lipid oxidation is shown by an increase in the lag phase for conjugate diene production which was 60 .+-. 15 min in the absence and 120 .+-. 20 min in the presence of 4 .mu.g/ml AS extracts ($p < 0.001$). TBARS production was reduced by 95% after 3 h incubation at 5 .mu.g/ml. Aggregation of apoB was abolished at the same concentrations. SIN-1 (3-morpholinosydnonimine) produces **peroxynitrite** via generation of NO and O(2)-. When LDL was incubated in its presence, a milder oxidation was observed as compared with Cu(2+), and AS produced over 70% inhibition. Finally, we show a striking dose-dependent inhibitory effect of lipoxygenase conjugate diene production, which is over 95% at AS concentrations of 5 .mu.g/ml. When compared with other antioxidants, AS effect is greater but in the same order of magnitude than that of ascorbic acid and similar to the popular herbal tea Ilex paraguariensis. In all three systems employed an effect is already substantiated at a concentration of the AS extract of 4 .mu.g/ml, which corresponds to a 1:100 dilution of the preparations usually drunk. .COPYRGT. 2002 Published by Elsevier Science Inc.

L4 ANSWER 1 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO Nature Neuroscience, (2002) 5:4 (283-283).
Refs: 1.
ISSN: 1097-6256 CODEN: NANEFN
TI A proposed mechanism of ALS fails the test in vivo.
AU Orr H.T.
PY 2002
AB In contrast to prevailing hypotheses, a genetic study shows that the toxic gain of function associated with mutant superoxide dismutase in familial amyotrophic lateral sclerosis is unlikely to be due to changes in its oxidative activity causing an increase in free radicals.

L4 ANSWER 2 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO Drug Development Research, (1 Jul 2002) 56/3 (290-292).
Refs: 108
ISSN: 0272-4391 CODEN: DDRESM
TI Progress in the development of new treatments for combined Alzheimer's and Parkinson's diseases.
AU Masliah E.; Hansen L.A.; Rockenstein E.; Hashimoto M.
PY 2002
AB Misfolding of synaptic molecules such as amyloid .beta. peptide and .alpha.-synuclein has been proposed to play a key role in the mechanisms

of neurodegeneration in Alzheimer's and Parkinson's disease, respectively. Notably, the majority of patients with Alzheimer's disease also have .alpha.-synuclein-immunoreactive Lewy bodies, and a substantial proportion of them develop a form of parkinsonism also known as Lewy body disease, that defies conventional therapies. Thus, factors involved in the pathogenesis of Alzheimer's disease might promote the development of particularly recalcitrant forms of Lewy body disease. We have shown that the amyloid .beta. peptide 1-42, of Alzheimer's disease, promotes the toxic conversion of .alpha.-synuclein and accelerates .alpha.-synuclein-dependent deficits in transgenic mice. Understanding the mechanisms promoting the toxic conversion of .alpha.-synuclein is of critical importance for the design of rational treatments for Lewy body disease and transgenic models hold the promise for the development of such novel therapies. In this context therapies aimed at: (1) reducing amyloid .beta. peptide 1 - 42 production, (2) blocking toxic .alpha.-synuclein oligomerization (e.g., .beta.-synuclein, antioxidants), (3) promoting .alpha.-synuclein protofibril degradation, and (4) protecting neurons (e.g., anti-oxidants, neurotrophic agents) against toxic .alpha.-synuclein aggregates might prove to be significantly useful in the treatment of Lewy body disease. We characterized .beta.-synuclein, the non-amyloidogenic homologue of .alpha.-synuclein, as an inhibitor of aggregation of .alpha.-synuclein. Our results raise the intriguing possibility that .beta.-synuclein might be a natural negative regulator of .alpha.-synuclein aggregation, and that a similar class of endogenous factors might modulate the toxic conversion of other molecules involved in neurodegeneration. Such an anti-amyloidogenic property of .beta.-synuclein in combination with other treatments might also provide a novel strategy for the treatment of neurodegenerative disorders. .COPYRGT. 2002 Wiley-Liss, Inc.

L4 ANSWER 9 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO Biochemical Journal, (1 Oct 2002) 367/1 (169-178).
Refs: 49
ISSN: 0264-6021 CODEN: BIJOAK
TI Biphasic translocation of Bax to mitochondria.
AU Capano M.; Crompton M.
PY 2002
AB Using green fluorescent protein-tagged Bax, we demonstrate that Bax is sequestered from the cytosol of cardiomyocytes in two distinct phases following the induction of apoptosis with staurosporine. In the first phase, lasting several hours, Bax removal from the cytosol was relatively small. In the second phase, Bax was very largely removed from the cytosol and sequestered into large aggregates associated with the mitochondria. To test which of the phases involved **cytochrome** c release, cells were transfected with a red fluorescent protein-**cytochrome** c fusion. The **cytochrome** c fusion protein was accumulated by mitochondria of healthy cells and was released by staurosporine in phase 1. When green fluorescent protein-Bax was immunoprecipitated from extracts of cells in phase 1 and phase 2, the voltage-dependent anion channel (mitochondrial outer membrane) and the adenine nucleotide translocase (mitochondrial inner membrane) were also precipitated. These data support a two-phase model of Bax translocation in which Bax targets the mitochondrial intermembrane contact sites and releases **cytochrome** c in the first phase, and is then packaged into large aggregates on mitochondria in the second.

L4 ANSWER 10 OF 95 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO FEBS Letters, (24 Apr 2002) 517/1-3 (133-138).
Refs: 21
ISSN: 0014-5793 CODEN: FEBLAL
TI Nuclear Apaf-1 and **cytochrome** c redistribution following

stress-induced apoptosis.
AU Ruiz-Vela A.; Gonzalez de Buitrago G.; Martinez-A C.
PY 2002
AB Apoptotic protease activating factor-1 (Apaf-1) and **cytochrome** c are cofactors critical for inducing caspase-9 activation following stress-induced apoptosis. One consequence of caspase-9 activation is nuclear-cytoplasmic barrier disassembly, which is required for nuclear caspase-3 translocation. In the nucleus, caspase-3 triggers proteolysis of the caspase-activated DNA nuclease (CAD) inhibitor, causing CAD induction and subsequent DNA degradation. Here we demonstrate that apoptotic cells show perinuclear **cytochrome** c aggregation, which may be critical for nuclear redistribution of **cytochrome** c and Apaf-1. We thus indicate that the nuclear redistribution of these cofactors concurs with the previously reported caspase-9-induced nuclear disassembly, and may represent an early apoptotic hallmark. .COPYRGT. 2002 Published by Elsevier Science B.V. on behalf of the Federation of European Biochemical Societies.

=> s l4 and (cytochrome c)
L5 53 L4 AND (CYTOCHROME C)

=>

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